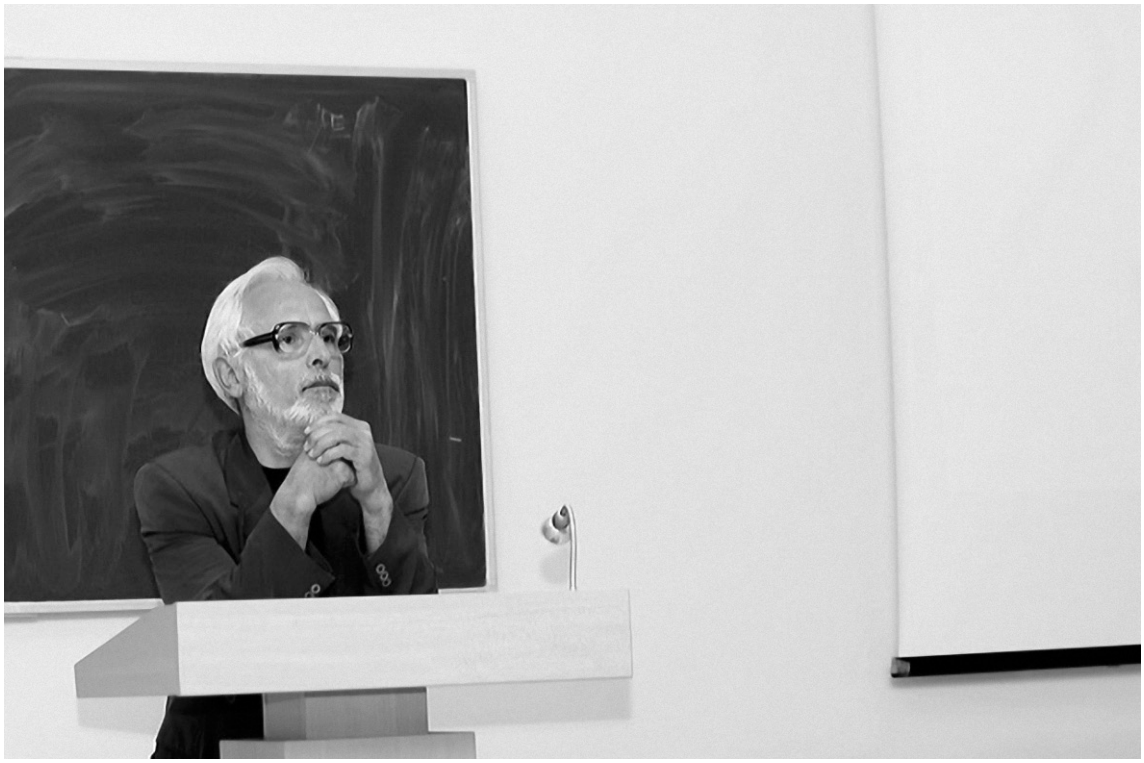
GEORGE 50
Years in Research



GEORGE 50
Years in Research
An autobiographical sketch

George N. Chaldakov

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Varna, 2012

This book is dedicated with respect and love to my parents, teachers and friends, including my family.

George

Piglet sidled up to Pooh from behind.
- Pooh? - he whispered.
- Yes, Piglet?
- Nothing - said Piglet, taking Pooh's hand.
I just wanted to be sure of you.

Alan Milne, *Winnie-the-Pooh*

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Front cover: *Friendorama,* a "periodic table" friends. In analogy with Dimitri Mendeleev's Periodic Table of molecules, empty boxes predict the appearance of new friends. The *Friendorama* is made by Vesselka Nikolova and Kiril Todorov.

Contents

Acknowledgments

Zenon learned from Parmenides of Elea, Plato – from Socrates, Aristotle – from Plato, Alexander the Great of Macedon – from Aristotle, Friedrich Nietzsche – from Fyodor Dostoyevsky, Carl Yung – from Sigmund Freud, Salvador Luria [1], Renato Dulbecco [2] and Rita Levi-Montalcini [3] – from Giuseppe Levi, Luigi Aloe – from Rita Levi-Montalcini, Marco Fiore – from Luigi Aloe, Hristo Photev [4] – from Ivan Peychev [5], Petya Doubarova [6] – from Hristo Photev…

The author of *George 50* – from his parents, teachers and friends.

That is the high tide of hierarchy in action,
From the groan to the sigh - to the echo… (Hristo Photev)

I cordially thank Stoyan Stoev, MD and Danko Georgiev, MD, PhD for critical reading of the manuscript.

List of abbreviations

ABC, amico, banca e capo (Italian, friend, bank and chief)
ACAP, as creatively as possible
BDNF, brain-derived neurotrophic factor
BGSCB, Bulgarian Society for Cell Biology
BHF, brain-and-heart friend(ship)
BHFF, brain-and-heart friend forever
BMF, Biomedical Forum
BMI, body mass index
BMI, brain mass index
BMR, *Biomedical Reviews*
CNR, Consiglio Nazionale delle Ricerche (Italian, National Research Council)
ISAA, international symposium on adipobiology and adipopharmacology
LD, liquid discussion
LLP, library-laboratory-pub
MT, microtubules
NGF, nerve growth factor
RLM, Rita Levi-Montalcini
SEM, scanning electron microscopy
SMC, smooth muscle cell(s)
SOS, state-of-the-science
TEM, transmission electron microscopy

1 - 3 Warded the Nobel Prize in Physiology or Medicine in 1969, 1975 and 1986, respectively.

4 - 6 Great Bulgarian poets: Photev (1934-2002) and Doubarova (1962-1979) lived in Burgas.

PROLOGUE

*I am I and my circumstance***.**
José Ortega y Gasset, *Meditaciones del Quijote*, 1914

In the life of each individual, "I" (human being) can not be detached from "my circumstance" (surrounding world). This led the most famous Spanish philosopher Ortega y Gasset to pronounce his famous maxim *Yo soy yo y mi circunstancia*. In the language of current biomedicine, this may be expressed by the concept of exposome, Gema Frühbeck and I *Dance Round* in *Adipobiology* [1]. As well as by Antonio Gomez Rufo's "The soul weights as much as soul's memories weight", written in his book "The soul of fish".

Programmed by my parents, the project of my life started on 23 February [2] 1940 in our family house in 27 Slivnitsa Street in Burgas, a city "sitting on the dock of the bay" (title of Otis Redding's song) of Bulgarian coast of Black Sea. Since then now at the age of 72, my parents, teachers, friends and I have been staying perfect together.

In the paradigms of cultural topology and anthropology, South-North, Mediterranean-Gothic and Apollonian-Dyonician individuals are phenotypic expressions of different style of behavior, including self-identification and attachment to or detachment from the relatives, friends and native place – *numen inest* (there is a spirit here) as appeared in the poem *Fasti* (Roman Calendar) by Ovid(ius), an ancient Roman poet.

Likewise, *genius loci* (spirit of a place), a natal philopatry, a geomagnetic imprinting (like that featured the natal homing in salmon and sea turtles). A sentimental topology - one has to have receptors for home adhesion molecules (like lymphocyte-endothelial interaction) to transmigrate from social circulation to native place, to see parents, sit around the table of his/her mother and enjoy feelings of togetherness – simply, to target himself to proper places and proper people, to do things properly. And virtuously.

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1 Frühbeck G, Chaldakov GN. Would-be-worlds of adipobiology in the exposome of globesity. *Adipobiology* 2012; 4:107-110.

Professor Gema Frühbeck (Department of Endocrinology and Nutrition, University of Navara, Pamplona, Spain) is a daughter of Rafael Frühbeck de Burgos, a chief conductor of almost all the big orchestra in the world, since 2012 appointed of the Danish National Symphony Orchestra. This should be the main reason Gema call me Chaldakov de Burgas.

2 Etymologically, from Latin, *februa* means "instruments of purification", an explanation I found in the poem *February (Book 2)* from *Fasti* of Ovid.

Douglas Noel Adams, the author of *The Hitchhiker's Guide of the Galaxy*, once said he was proud that the abbreviation of his names is DNA and that he had been born in Cambridge one year before DNA discovery. However, 23 of February may also be linked to a "how good and yet how sad" story related to the discovery of DNA structure. It was 13 years later when I was born: on (or around) 23 February, Francis Crick and James Watson completed the model of double-helix structure of the DNA molecule in Room 103 of Cavendish Laboratory in Cambridge University. After that they went in the pub *The Eagle* and announced to their friends that they had discovered "the secret of life". Crick and Watson then published their DNA model in *Nature* on 25 April 1953 with only a footnote acknowledging "having been stimulated by a general knowledge" of Franklin's unpublished contribution. Although they had enough specific knowledge of Franklin and Gosling's data including their famous *Photograph 51* of X-ray diffraction image of DNA taken in 1952, upon which Crick and Watson based their "own" model.

This is why Diogenes said: *Ethica quaero*, a paraphrase of his *Hominem quaero* (Latin - looking for an honest man).

Arhimedes' *genius loci* was Syracuse, Sicily in *Magna Grecia*, Castilla-La Mancha – of Don Quixote *and* Sancho Panza, Arl – of Vincent van Gogh, "Salamanca is a big metaphor" of Miguel de Unamuno, Tahiti – of Paul Gauguin, Granada – of Federico Garcia Lorca, Dublin – of James Joyce, Buenos Aires – of Jorge Luis Borges, Araka-taka, which became Macondo in *"*One Hundred Years of Solitude*"* – of Gabriel Garcia Marques, Amantea in Calabria, Southern Italy – of Luigi Aloe, Burgas – of Hristo Pho-tev, Varna – of the philosopher Alexander Stoychev, Kalimanitsa – of Yordan Radi-chkov, a famous Bulgarian novelist and playwriter.

Burgas is *genius loci* of George 72, as described in the essays published in 2012 in his book *Burgas. Sentimental Stories* (in Bulgarian).

The Latin poet Virgil wrote that "the Earth is God's creation, while the city is man's creation", also *axis mundi* (the center of world). Mount Fuji symbolizes the world axis in Japanese culture, particularly when you are sitting on Fuji's feet and watching how the snail of Kobayashi Issa

Climb Mount Fuji,
But slowly, slowly!

Vatashi-no-michi (Japanese - My way), namaoke, a subtype of karaoke, bar, owned and moved by Yuasa san and his wife, was my *axis mundi* of Izumo, Shimane prefec-ture in Japan (1986-1987). Later I wrote: In "My way" in Izumo was delightfully to listen Frank Sinatra's "I did it my way".

The George, a pub near the Royal Free Hospital School of Medicine, was my *axis mundi* of London in England (1991-1992).

Noppo (Japanese, Tall), a restaurant near medical school, owned and moved by Sadao san, a tall and noble man, was my *axis mundi* of Kanazawa in Japan (2003-2004), especially when sitting at the bar with Tomiko san, a lady over 90 years of age, and drinking *sake* together.

Amantea, *una bellissima cittadina* (Italian, a beautiest small town) located the south of Italy close to the west cost of the Mediterranean see, the native place of Dr Luigi Aloe, is my *axis mundi* of Italy (1998-now), particularly Ferdinando's restaurant "The Paradise".

Burgas's *axis mundi* for me is the streets near the native house we used to play as children, the schools we studied, and the pubs we drank, especially *The Casino* moved by my father (will further write about).

Similar to Aristotle's "the whole exists before its parts", Miguel de Unamuno in his book *Our Lord Don Quixote* wrote, paraphrasing: "City's soul creates the person. A per-son is nothing but an individualized collective soul." Though, Jorge Luis Borges argued that person's soul creates the city. As, for example, *corrida* (bullfighting) described by Ernest Hemingway in *The Sun Also Rises* created world popularity of Pamplona, Dr Gema Frühbeck's native city.

Last but not least, "If you are lucky enough to have lived in *Burgas* as a young man, then wherever you go for the rest of your life, it stays with you, for *Burgas* is a move-able feast" - Hemingway wrote in his book *A Moveable Feast. Sketches of the author's life in Paris in the twenties*.

Salutationem Vobis Facio in Burgas (Greetings to everybody in Burgas)!

MONOLOGUE OF A SON

Ay mamá, ¿cómo pude
vivir sin recordarte
cada minuto mío?
No es possible.

Mother, how can
I live without recalling you
Every minute of mine?

That is impossible – continued the great Pablo Neruda in his poem *La mamadre*.

In the first days of the 20th century, the father of my mother Ivan K. Papucharov (1884-1957) arrived in Burgas from Chepelare, a town in the Rhodope Mountains in Southern Bulgaria. He has later built many buildings and houses in the city including our family house on 27 Slivnitsa Street in a central area of Burgas.

"The husband of my mother loves me very much", wrote Nicaraguan poet Ernesto Cardenal. My father Niko S. Chaldakov (1908-1976) arrived in Burgas at the age of 10-11 from a small village near Burgas. Starting as servant in shops and pubs, later he has developed his own pub and named it "Niko's Family Aperitif" – in 1947 it was nationalized by the commies. Since then my father continued work as Executive Director of restaurants. From 1951 to 1970 he run *Morsko casino* (Sea casino). Many clients called my father "Uncle Niko", a sign of mutual respect and understanding. Thus I was much popular in Burgas as the son of Niko Chaldakov than Dr Chaldakov. Now when we walk the streets of Burgas together with my grandson Nikifor (after the name of my father and my son Nikolai), old men say: "Look, these are the son and the great grandson of Niko Chaldakov" – a sign of the most sentimental respect in one's life.

According to my father explanation, the etymology of our family name Chaldakov derived from the Turkish word "chaldak" meaning "will do that for you; you will have it." During the time of Ottoman (Turkish) occupation of Bulgaria (1395-1878), when our great grandfathers entered the pub, they asked musicians to play a song for them. And musicians replied: "Chaldak".

A comment of my friend on this etymological story is: "Chaldak" is a nice word indeed, it sounds like performed promise."

THE CASINO: *NUMEN INEST* OF BURGAS

In 1879, a year after the liberation of Bulgaria, there were about 1 200 houses in Burgas, a city with a population of 2 490 people. Then, the first Mayor advised citizens of Burgas to open more pubs and cafes to stimulate people's fun. In medical terms, the Mayor prescribed one of the best remedies – *joie de vivre* (enjoy life).The citizens followed carefully the prescription and in 1888 there were 155 registered pubs at the disposal of 9 865 inhabitants, that was, a pub per 63-64 people. On 28 August 1938, a remarkable event has been happened in Burgas: the Bulgarian minister of education has opened the restaurant *Morsko casino*, an event that has not been happened even in the majestic realism of Gabriel Garcia Marquez. Since then *The Casino* became the "school" of choice in Burgas. For about 20 years my father managed excellently *The Casino*. After his own pub *Niko's Family Aperitif*, *The Casino* became his second *magnum opus*. This is way he was promoted to Full Professor of Pubs.

The Casino was the only restaurant in Burgas working until 2 AM, thus being a cherished place of artists, poets and other Dionycian type people. Recently, it was restored and on 26 March 2011 officially launched as Cultural Center "Morsko casino", preserving the name because "there is spirit here"(*numen inest*). Altogether, this sentimental retrospect motivated our decision to select the Cultural Center "Morsko casino" for the venue of the 3rd Third International Symposium on Adipobiology and Adipopharmacology (ISAA), 25 - 27 October 2012. Scientists with very high BMI (brain mass index) from 17 countries will present their state-of-the-science (SOS) lectures.

1960: "WHAT DID I ARRIVE HERE FOR?"

In 1957 I graduated *summa cum laude* from high school in Burgas, and applied for Medical Institute in Sofia (the capital city of Bulgaria), but having no commie administered privileges was not admitted. Nor was I "approved" as fit – because was young - for military service. That was the reason why during the "academic year" 1957-1958 I worked in a food-producing factory in Burgas making (and consuming) biscuits.

During this time, due to the lectures of my second cousin and a great friend Peter Petrov, a highly tuned intellectual renowned in Burgas by his nickname *Mosakat* (The Brain), I was introduced to the pub auditoria and thus enrolled as students in the University of Life Sciences. Here I contacted famous theatre artists, poets, lawyers, physicians, ship's captains and sailors, and for the first time started to drink, preferably red wine. *The Casino* of my father was the preferable auditorium for these interactive lectures.[1] Although welcomed us, my father had quite different opinion about this type of education.

From 1958 to 1960 I have served my required time in the Bulgarian army and then applied again for student in Sofia Medical Institute, also Faculty of Law at State University of Sofia. My parents did like to become medical doctor or lawyer. Now it was with entrance exams in chemistry and biology (for medicine) and Bulgarian literature and history (for law), which I passed excellently, and was admitted in both Medical Institute and Faculty of Law. I selected medicine and started the preparation to go in Sofia. My father, keeping in mind that I used to join the company of people who enjoy drinking, gave me a table (27 to 16 cm) – on blue background was calligraphically written in red: WHAT DID I ARRIVE HERE FOR? Then he told me: *When your friends call you to drink, read the message. The answer is to study, not to drink!*

To better memorize, my mother repeated it, and in September 1960, the message and I went in Sofia. I did follow it and thus attended the lectures and seminars, took the exams (semi)excellently, and came "now is the time to drink" (Latin, *nunc est bibendum*) with friends in pubs. Hristo Photev, an emerging that time as great lyric poet, introduced me and my girlfriend Antoaneta, a dentistry student (since 1966 now my wife), to *Cafe Bambuka* (Bamboo). Key regulars included famous Bulgarian poets, writers, artists and other intellectual bohemians. Thus we, the teenagers, met with the great Bulgarian poet and playwriter Ivan Peychev (1916-1976) and the emerging as great Konstantin Pavlov (1934-2008), who became one of Bulgaria's most prominent intellectuals with his wisdom poetry, metaphoric screenwritings and rare defiance of the country's 1944-1989 communist regime. Sometimes, the uncle of Antoaneta, one of the leading Bulgarian mathematicians, Blagovest Dolapchiev, invited us to lunch in *Russian Club* or *Czech*

1 Of many lessons I learned, I remember some from "Decalogue of Burgas bohemian": (*i*) make your dreams memories, (*ii*) there are no prostheses for mind and soul, (*iii*) the real man does not rely on one work, one woman, one drink, (*iv*) *Dum bevo spero* (While I drink, I hope) sounds better than *Dum spiro spero* (While I breathe, I hope), and (*v*) if you have no money for bread, buy wine.

Club, where we met other famous Bulgarian intellectuals. It was *joie de vivre* and *carpe diem* (seize the day) indeed.

In such a way, from exam-to-pub, not from pub-to-exam, our student life was effectively and joyfully processed – 2 years in Sofia (1960-1962) and the remainder of 4 years in Medical Institute of Varna (in 1990 renamed Medical University).

Since then now, WHAT DID I ARRIVE HERE FOR? has been playing a role model of my behavior. In the early 1990's, when he studied art photography in London, UK, I gave the message to my son. Now I am showing it to my grandson Nikifor (9) and when he matures his father will give the torch to him…

I call that "the flow of genes and memes" [2] – *perpetuum mobile de vita*.

1962-1966: HOW I BEGAN OR, LLP PATTERN OF RESEARCH

In Sofia, I had a chance to be in the classes of biochemistry led by Dr Assen Hadjiolov Jr, who later became worldwide recognized biochemist in RNA research. His lessons did provoke my curiosity (Bulgarian, *lyuboznanie* - a symbiosis of "love" and "knowledge") in cellular and molecular biology.

In September 1961, Medical Institute of Varna was launched with students in 3rd year - all students from Eastern Bulgaria were obligatory translocated from Sofia to Varna. In the academic year 1962-1963 we have to also move to Varna. Then I told Dr Hadjiolov that like to be involved in biochemistry research in Varna. He advised me that the best place for that is the Department of Pharmacology chaired by Professor Delcho Zhelyaskov. In September 1962, I arrived in Varna and immediately contacted Professor Zhelyaskov asking him to accept me as a research associate at his department. He involved me in the study of substrate and organ heterogeneity of monoamine oxidases (MAO) supervised also by Dr Petko Uzunov, an Assistant Professor that time. During my 4 years in Varna, I spent at least 1-2 hours daily in the library and 2-3 hours daily in the laboratory, measuring MAO activity in rat liver and brain homogenates. Thus kept myself on what I designated "triarchic pattern of research", that is, library-laboratory-pub (LLP). Regarding the first element of LLP, since 1962 onward, most of the core international biomedical journals were available in Bulgaria, and one's curiosity can, via post mail, request articles-of-choice published worldwide, despite of "Big Brother is watching you", a reminiscent of *Nineteen Eighty-Four*, a 1949 novel by George Orwell. Regarding the second element, there is a Bulgarian proverb saying "who likes to be a servant, has to find his Master" – I looked for and found him, Professor Zhelyaskov became my Master. Regarding the third element, there are many pubs, select friends to visit some of them, a remark of *E pluribus unum* (Latin, out of many, one), first articulated by old Roman philosophers and poets, and much later appeared on the Great Seal of the USA.

2 To emphasize commonality with gene, a unit of biological transmission, the word *meme,* a unit of cultural transmission, originated with the British evolutionary biologist Richard Dawkins' 1976 book *The Selfish Gene* (some scientists named this hypothesis "pseudoscientific dogma"). Dawkins coined the term "meme" by shortening "mimeme", which derives from the Greek word *mimema* (something imitated). Memes, "the cultural DNA", vary in their aptitude to replicate - memes that are good at getting themselves copied tend to spread and remain, whereas the less good ones have a higher probability of being ignored and forgotten. Thus the better memes are selected, the evolutionary dreams become reality.

But not always, and diseases are developed, one of them being arrogant behavior upregulated in some scientists. This is why, I wrote to the author of *The Selfish Gene* that someone will soon write a book titled *The Arrogant Richard Dawkins*. Or, *The Arrogant T.Y. and N.M.*

In sum, there are lots of potentials in the elements, one has to explore them creatively. More importantly, the LLP pattern does require passion, "intellectual passion, passion for discovery and exploration: the mightiest of all passions", quoting "another George", George Bernard Shaw. Recently, Sir Ken Robinson's 2009 book "The Element" also dealing with "how finding your passion changes everything".

Certainly, I did not attend any lectures out of the scope of my curiosity, for example, hygiene, obstetrics and gynecology, ophthalmology. Because in the laboratory I captured more important messages and knowledge than in the auditorium. At the laboratory I also learned how to present own findings to scientific meetings and journals; in 1965 was selected to present our findings at the international student conference in Łódź, Poland. It was my first trip abroad.

In effect, at the Department of Pharmacology my curiosity, a wonderful gift from my parents, was enriched with the devotion to biomedical research due to Professor Zhelyaskov and Dr Uzunov, my scientific fathers.

LYUBOZNANIE IS A WONDERFUL WORD

As I wrote, *lyuboznanie* is a symbiosis of "love" and "knowledge" in one word - in, perhaps, Bulgarian language only. Something like "fallen in knowledge" - when two words are met for the first time, a poetry is born. Or, "it's like a portmanteau - there are two meanings packed up into one word" – said Humpty Dumpty's to Alice in Lewis Carroll's *Through the Looking Glass*.

Another wonderful Bulgarian word related to *lyuboznanie* is *lyubomadrost* - a symbiote of "love" and "wisdom". Something like "fallen in wisdom". Semantic friends of these two Bulgarian words are (*i*) the Greek φιλοσοφία (*philosophia*) - "love of wisdom", and αρήτη (arete) - all kinds of virtues leading to excellence (ἀρετή), (*ii*) the Greek phrase Φιλοσοφία Βίου Κυβερνήτης (*philosophia biou kybernētēs*) - "Love of learning is the guide of life" abbreviated *Phi Beta Kappa* (ΦΒΚ), and (*iii*) the Latin *sapere aude* - "dare to be wise" or, "have the courage to use your own mind", originally used by Roman poet Horace and centuries later, on 30 September 1784, associated with Immanuel Kant's *An Answer to the Question 'What Is Enlightenment?"*

The words *lyubomadrost* (noun), *lyubomadar (*adjective, singular*),* and *lyubomadri* (adjective, plural) were used (perhaps, introduced) by Paisii Hilendarski (Paisius of Hilendar Monastery), the father of Bulgarian renaissance, the first ideologist of the national liberation movement. The first Bulgarian to feel the tendencies for development of the society undertakes the role to awake the national conscience by writing "History of the Slavs and Bulgarians" released just 260 years ago, in 1752.

"Attention here, *lyubomadri* reader, to use this knowledge for a clever delight and for the benefit of yourself and others" – Paisii Hilendarski wrote in "The History". Sounds very similar to Horace's *Lectorem delectando pariterque monendo* (enjoy the reader and teach him) in his *Ars Poetica, line 343*.

Today*,* Carl Djerassi, a Bulgarian Jew*,* Emeritus Professor of Chemistry at Stanford University, and one of the discoverers of contraceptive pills (colloquially known as "the Pill"), applied Horace's and possibly Paisii's thoughts in writing his dramas (e.g., "Oxygen/O_2" and "NO") and novels. Accordingly, he introduced the terms *science-in-theater* and *science-in-fiction*, respectively. The present "George 50" might be considered a kind of *science-in-fiction*. As well as my essays collected in the book "The Butterfly and the

Blue Pill" (the latter not related to any aphrodisiaca) - now in press.

1967-1970: GP DOCTOR

I graduated from Varna Medical Institute in December 1966. Because we studied 2 years in Sofia followed by 4 years in Varna, I used to say that we are a hybridoma generation. Although none of us was awarded Nobel prize as hybridoma technology for monoclonal antibodies production achieved in 1975 for its inventors, Ceasr Milstein, Georges Köhler and Niels Kaj Jerne. This is why on 17 January 1967 I began my GP doctor practice in 4 villages near the city of Karnobat in District of Burgas. Two weeks later, on 31 January 1967, my son was born in Burgas, my wife cared for him 2 years, and later joined me for only a year doing dentistry. When we are meeting now people from these villages, they tell they remember us.

My fellow-students became renowned university scientists and teachers: Michail Davidoff is the best Bulgarian cell biologist, last 20 years working in Hamburg, Germany, now Emeritus Professor at the Anatomical Institute of Hamburg University, author of the concept of neuroendocrine nature of testicular Leydig cells and of pericytes as ubiquitous adult stem cells; Stoyan Stoev is the best in forensic medicine used to teach students in Sofia and many countries abroad - his sentimental geomagnetism returned him to the native Burgas; Kamen Uzunoff was the best in tracing brain neuronal connections (today's connectomics), taught students in Sofia and used to work in Germany and The Netherlands; Slavi Slavov is the best allergologist and taught student in Sofia; Ivan Stankulov was the best in forensic medicine and taught student in Varna Medical University; Stansilav Yanev is the best in pharmacology and toxicology, working in Bulgarian Academy of Sciences; Assen Jablensky is the best phsychiatrist, last 20 years working in Australia, now Director of Center for Clinical Research in Neuropsychiatry at The University of Western Australia in Perth.

I worked 3 and a half years as a GP doctor - it was a required time of at least 3 years after the graduation each MD to work in a village health service. To stay tuned with the current information flow in pharmacobiochemistry, I continued my talk with the medical libraries in Varna and Sofia. And ordered journals in accordance with my *Iyuboznanie*.

1970: RETURN TO *ALMA MATER*

In March 1970, my scientific fathers informed me that Laboratory of Electron Microscopy is launched at Medical Istitutue of Varna. They advised me to apply for the announced position of research associate. Passing the exams on cell ultrastructure and English language, I won the position among 6-7 candidates and returned to *Alma mater studiorum* in Varna. In July 1970 I was appointed research associate at the Laboratory. Colleagues from all departments came there and I taught them to apply the methods of transmission electron microscopy (TEM).

I myself started with the ultrastructural study of human brain tumors. However, the head of Laboratory, also Department of Neurology, was a not well educated, "red" professor I could not tolerate his mentality. This is why in January 1972 I moved to Department of Anatomy and Histology where the main research topic was the structure of vascular wall.

1972-1992: TEM STUDIES IN SMOOTH MUSCLE CELLS

To be a scientist *is profound responsibility*.
Paraphrase from Emily Dickinson's *To be a flower*

During the 1970s, TEM was a sophisticated technology for studying cell structures and functions. Using JEM 7A electron microscope, my colleagues and I produced good quality of electron micrographs supporting our hypothesis of the secretory function of vascular smooth muscle cells (SMC).

In 1960, Dr Maria Daria Haust and colleagues published their pioneering results of fibroblast-like potential of SMC. For conventional thinking these data were shocking because "the normal science" mandated that the sole SMC's function is contraction-relaxation, and that fibroblasts are in charge only to produce matrix fibrous structures in the vascular intima affected by atherosclerosis. As happened in the history of (biomedical) science, such an ignorance was, most probably, a result of an epistemological break (in sense of Gaston Bachelard) induced by the great pathologist Rudolf Virchow's dogma that lasted about 100 years. For instance, when a young German pathologist, Theodor Langhans, reported his observations of stellate cells in human atherosclerotic plaques, suggesting they are not fibroblasts, as Virchow believed, his data were ignored. Until 1960 when Daria Haust recognized these cells as SMC [1]. Later, in her book about SMC in atherosclerosis, she wrote that the only thing Langhans missed to report was that the stellate cells he observed were, in fact, SMC. In effect, Haust's findings planted the modern seeds of paradigm shift (in sense of Thomas Kuhn's 1962 *The Structure of Scientific Revolutions*) in SMC biology of atherosclerosis.

Based on the works of Daria Haust, Russell Ross, Andrew Somlyo, Julie and Gordon Campbell, Geoffrey Burnstock..., in the early 1970's the concept of SMC phenotypic modulation has emerged. Accordingly, SMC having less actin and myosin filaments but rich in endoplasmic reticulum and Golgi complex were designed "modified SMC" and later, "synthetic SMC" and "secretory SMC". Epistemologically, how long this modern doctrine will last and whether will malignate into dogma is a matter of another autobiographical sketch.

In 1972, I was a newcomer in the field and thus free of Virchow's syndrome, whereas full of *Iyuboznanie*. Hence, applying LLP pattern of research, I started to carefully pursued the TEM observations on exocrine pancreatic secretion published by the wonderful George Palade. There were my *Libro d'Oro* (Golden Book), and I did absorb its data and concepts in, perhaps, more details than Palade himself, as I told him in 1982 when we met during the World Congress of Physiology held in Budapest, Hungary. In fact, Palade's findings created the current knowledge of cell protein secretion, particularly endoplasmic reticulum-Golgi complex secretory pathway, which brought him the 1974 Nobel Prize in Physiology or Medicine shared with Albert Claude and Christian De Duve.

According to phenotypic modulation, there are two major states of SMC: contractile and synthetic state. Being an excellent *in libro* student of George Palade, we introduced the term "secretory state SMC" instead of "synthetic state SMC" - because synthesis is just an initial step of the secretory pathway. Consequently, "secertory state

1 Haust MD, More RH, Movat HZ. The role of smooth muscle cells in the fibrogenesis of arteriosclerosis. *Am J Pathol* 1960; 37: 377-389.

SMC" were appreciated by the colleagues in vascular biology community.

"One should not say "I think". One has to say "I was taught" – wrote the famous poet Arthur Rimbaud, on 13 May 1871 in a letter to his teacher in Charleville, his native town in Northern France. According to Mark Twain, Adam only knew that everything he said is for the first time. Later this thought was developed by Carl Jung who wrote: *Ask yourself for each of your thoughts: is it a new one?*

Now I may cautiously share with you that in vascular SMC, we have for the first time described (*i*) Golgi-derived secretion granules, (*ii*) cytoplasmic microtubules, and (*iii*) plasma membrane-derived coated vesicles, as structural components of protein cell secretion and receptor-mediated endocytosis, respectively [1-6]; these were the main topic of my PhD Thesis defended in 1983. More importantly, our findings were described and conceptualized in 1982 Letter to Editor[4] and in 1986 review[5] both published in *Atherosclerosis*, a core journal in the field.

"Enough for one early Sunday morning", as Dr Jack P. Strong from New Orleans, LA wrote in a letter to me dated of 12 September 2010, describing the feeling of fun of Mihoko, daughter of the famous Japanese poet Ema Shoko. However, it was not enough for a small laboratory in a small country. Because my father taught me that a task performed calls for a new task to be performed.

1971: LIQUID LUNCH WITH DR ERMINIO COSTA

In 1971, annual meeting of the Federation of European Biochemical Societies (FEBS) was held in Varna. It was attended by famous scientists, one of them David Sabatini who

2 Chaldakov GN, Nikolov S, Vankov V. Fine morphological aspects of the secretory process in arterial smooth muscle cells. II. Role of microtubules. *Acta Morphol Acad Sci Hung* 1977;25:167-174.

3 Chaldakov GN, Nikolov S, Vankov V. Fine morphological aspects of the secretory process in arterial smooth muscle cells. I. Secretion granules. In: *Proc 19th Morphol Cong, Charles University, Prague*. 1978; 619-625.

4 Chaldakov GN. Antitubulins - A new therapeutic approach for atherosclerosis? *Atherosclerosis* 1982; 44: 385-390.

5 Chaldakov GN, Vankov VN. Morphological aspects of secretion in the arterial smooth muscle cell, with special reference to the Golgi complex and microtubular cytoskeleton. *Atherosclerosis* 1986; 61: 175- 192.

5 Chaldakov GN, Vankov VN. Antifibrotic approach in the therapy of arterial occlusive diseases: new considerations. In: G. Trubestein, editor. *Conservative Therapy of Arterial Occlusive Disease*. Stuttgart, New York, Georg Thieme Verlag, 1986, p. 224-226.

6 Chaldakov GN. Anti-inflammatory drugs and ischemic heart disease: new considerations (a cell biologist's proposal to cardiologists). *J Am Coll Cardiol* 1991;17:1445-1446. To evaluate the role of cytoplasmic microtubules (MT), we administered (to rabbits at different age) colchicine, a MT-disassembling (antitubulin) agent, and found a significant aggregation of secretion granules around the Golgi complex suggestive for the role of MT in the intracellular transport of these granules. In 1993, the first data by the group of George Cooper 4th have been published demonstrating that the excess density of MT is important for myocardial contractile dysfunction suggesting that this may be one mechanism contributing to the development of heart failure (HF) caused by cardiac hypertrophy. And that colchicine restored the contractile activity of cardiomyocytes. Today's data of Cooper's group enriched this paradigm (Cheng G, *et al*. Cytoskeletal role in protection of the failing heart by β-adrenergic blockade. *Am J Physiol Heart Circ Physiol* 2012;302:H675-687).

In brief, an old, but not yet answered, question is thus re-emerged: may colchicine and/or other antitubulins exert a therapeutic effect in both atherosclerosis and cardiac hypertrophy patients? Or, in the present drug war, colchicine and its derivatives are too cheap for pharmaceutical companies?

used to work at The Rockefeller University, New York, NY with Günter Blobel, the 1999 Nobel Prize Laureate for his signal hypothesis in protein targeting and sorting. I had a short talk with David. As neuropharmacology-sucked youngster, I mainly contacted scientists in that field. Unfortunately, had no courage to approach Dr Anika Dahlstöm from Karolinska Institutet, Stockholm, Sweden – she was too much charming! However, I contacted Dr Ermino Costa, a worldwide recognized expert in the field. He arrived in Varna from the Laboratory of Preclinical Pharmacology he chaired in the National Institutes of Mental Health at St. Elizabeth‘s Hospital, Washington, DC. Where one of my Varna scientific fathers, Dr Petko Uzunov, worked as visiting research fellow. Together with Dr Costa he studied the role of cyclic AMP and protein kinase A in the mechanism of action of psychotropic drugs.

Almost a year ago (in 1970), Dr Uzunov wrote me that he is arranging for me a position of visiting research fellow at Dr Costa's Laboratory. Thus, I very much like to talk with Dr Costa, as *capo di capi*, to authentically listen his personal opinion about. He welcomed me and invited me to lunch. During the walk to the restaurant, one of his first and, perhaps, key questions was: “Are you member of the communistic party?” I was not, and replied “No!” Hence, we had a friendly liquid lunch. Dr Costa told me that he is willing to indeed welcome me to his lab, within the next 2-3 weeks. This is fitted with what Dr Uzunov promised me.

But As “Tomorrow is a long time”, a song written and recorded by Bob Dylan, “2-3 weeks were a long time” too – I continued working in Varna, BG, not in Washington, DC. So much disappointedly, 2-3 years after my Varna talk with Dr Erminio Costa, I understood that it was not he who lied me, but my Varna scientific father. Since then I have been kept myself at a very long distance to him.

1973: MY FIRST TRIP WESTWARD

In the beginning of 1973, *Atherosclerosis* announced that the Symposium on the Smooth Muscle of the Artery will be held in October 1973 in Heidelberg, West Germany. Positions for 5 young scientists were available on a competitive pattern. The remainder of 45 scientists were the leaders in the field, most of them I have already been met *in libro*. The Organizers, the International Atherosclerosis Society (IAS), asked the candidates to submit CV and list of publications sharing his/her research focus to SMC as related to atherogenesis. Remembering Ernest Hemingway's “no penalty for winners”, I sent my documents without informing the head of Anatomy Department where worked. I knew that if informed him, he will not allow me to send the documents. Later when my application was accepted, I told him about. He bacame angry but Papa Hemingway said to me “Do not worry, George!” Most probably, the Organizers have listened to Papa, and scheduled my findings for a lecture presentation and covered all my expenses for the symposium, including a honorarium for my lecture (400 - Deutsche Mark were big money for a person with a monthly pay ranging 3-4 time less). In Heidelberg I understood that the personal recommendations of Daria Haust and Professors Olga and Yechezkiel Stein (Lipid Research Laboratory at Hadassah University Hospital in Jerusalem, Israel) also played a significant role for this positive decision. Since then they became my new scientific parents supporting me in other international events.

This is how a newcomer in the field appeared among the leading scientists in SMC research, including Daria Haust, Russell Ross, Robert Wissler, Andrew Somlyo, Julie and Gordon Campbell, Jack P. Strong, Geoffrey Burnstock, Laszlo Robert.... That is what I call “the excitement of moving from *in libro* to *in vivo*”. My lecture was programmed at

the beginning of the first session, after Russell Ross' talk, who shared his pilot data on platelet-derived growth factor (PDGF), which later became a famous biomolecule not only in the life of SMC.

The Organizers asked the speakers to submit their manuscripts for publication in *Adv Exp Med Biol* [1]. In the Chapter 1 under the title "Characteristics of Modified Smooth Muscle Cells" we described our finding in aorta and pulmonary trunk SMC of rabbits focusing on "secretory-contractile type SMC", a term we used that time. In this paper, along with the description of cytoplasmic MT and Golgi-derived secretion granules, "We propose the micro-pinocytotic coated vesicles as a new cytological sign of the modified SMC. One may speculate that both basement membrane and sarcolemma may be genetically endowed with properties for special uptake and transport of some macromolecules."

Though endocytosis via smooth-surfaced vesicles was first demonstrated in the 1950's by George Palade, before 1974, endocytosis was considered to be a nonspecific process that transported bulk fluid into cells. In 1975, studying familial hyperlipidemia, Michael Brown and Joseph Goldstein from the University of Texas in Dallas, in a collaboration with Richard Anderson, found at TEM level that low-density lipoprotein (LDL) coupled to electron-dense ferritin clustered into coated pits followed by the formation of plasmalemma-derived coated vesicle which internalized LDL-LDL receptor complexes for further intracellular processing in the regulation of circulating and cellular cholesterol homeostasis[2]. In 1985 Michael Brown and Joseph Goldstein were awarded the Nobel Prize in Physiology or Medicine.

Chairman of the Heidelberg symposium was Professor Schetler, President of IAS and a famous German cardiologist, co-chaired by Steward Wolf at the University of Texas, Galveston, TX and by Nicholas T. Werthessen at Naval Research, Boston, MA. Both scientific and social events were excellently managed including gala diner in *The Red Ox*. In this old restaurant, we began a new talk with Professor Jack P. Strong, Head of Department of Pathology, Louisiana State University Medical Center, New Orleans, LA. He asked me whether I like to work in his department. I, a dreamer for the USA, certainly had no other answer but *yes!* He told me I will be working also with Dr Herbert Stary, who is responsible for TEM laboratory. Dr Strong said to me that will send me an official invitation letter. His words were materialized in April 1974. The letter dated of 23 April 1974 started with "I am writing to confirm formally my invitation for you to join this department as a research associate for an initial period of one year." The letter enclosed a copy of Certificate of Eligibility for Exchange Visitor Status issued by Department of State.

"We shall be looking forward to having you join us", since 1 July 1974.

1974, 1975: AUTHORITY'S *NO* IN BIG-SIZED LETTERS

When I returned home from Heidelberg, I informed the head of our department that I was invited by Professor Strong to work in his department. He said to me "Yes, let you receive the official invitation letter." When the letter arrived, the same head of department

1 Chaldakov GN, Nikolov SD. Ultrastructure of modified smooth muscle cell. In: Wolf S, Werthessen NT, editors. *The Smooth Muscle of the Artery*. New York City: Plenum Press. *Adv Exp Med Biol* 1975; 57:14–20.

2 Goldstein JL, Brown MS. History of discovery. The LDL receptor. *Arteriosc Thromb Vasc Biol* 2009; 29: 431-438.

LOUISIANA STATE UNIVERSITY MEDICAL CENTER
1542 TULANE AVENUE •NEW ORLEANS • LOUISIANA • 70112

DEPARTMENT OF PATHOLOGY

April 23, 1974

Dr. George Chaldakov
Department of Anatomy
Faculty of Medicine
Varna, BULGARIA

Dear Dr. Chaldakov:

I am writing to confirm formally my invitation for you to join this department as a research associate for an initial period of one year. Your salary will be $10,000 per year from which there will be certain deductions for taxes, hospitalization, etc. After the initial appointment for one year there will be an option of extending the appointment for an additional year of mutually agreeable.

You will be supported by and working in our research program on atherosclerosis. In this regard we will expect you to investigate arterial lesions of experimental animals and humans using electron microscopy, histochemistry, and other methods of the laboratory. You will be working closely with Dr. Herbert C. Stary, Associate Professor of Pathology, who is responsible for much of the electron microscopy in our human and experimental studies.

I am enclosing a copy of certificate of eligibility for exchange visitor status in case you need this for your visa.

Please let me know the date that you expect to be in New Orleans.

We shall be looking forward to having you join us. Let me know if any additional information is required.

Best personal regards.

Sincerely,

Jack P. Strong, M.D.

Jack P. Strong, M.D
Professor and Head
Department of Pathology

JPS/kb
Enclosure
cc: Herbert C. Stary, M.D.

told me “No, I cannot allow you to go USA.” Such a metamorphosis is an example of the ugliest expressions of one’s words, behavior, mind. It is just such cases when Italians used to be less polite saying “grandissimo stronzo”.

Whatsoever, one was evident: my *Via dolorosa* has been paved in the cities of Varna and Sofia. During the commie regime, Bulgaria was a leading example of dystopian countries in Europe. For one to get passport for western countries, there were at least three “stations” to pass: agreement letter (*i*) from the head of department, (*ii*) from the rector of institute, and (*iii*) from the chair of communistic party committee of institute, a terrible triumpherat many of us suffered from. Being not a member of communistic party, I did not

get any of these letters, nor I received such a letter from the president of Medical Academy headquartered in Sofia, our institute being that time under its umbrella. This president was a brother-in-law of the Bulgarian leading commie dictator. A very authoritarian person who tyrannized the whole Bulgarian medical community. I did wait a front of his office every day of May 1974 until at long last he accepted me on the day 25th of my waitfulness. This vicious cycle ended with big-sized letters he used in his own handwriting of "NO" on my request letter. Telling me "You, the youngsters, always turn the eyes to western countries".[1] This was the fourth *NO* I received, which finalized my efforts to get permission to work in the USA. It still remains downloaded in the deepest layers of my mind.

Dr Strong whom I informed that I was engaged in teaching students and working on my PhD Thesis, both being false statements, because "Big Brother is watching you", sent to me the second invitation letter indicating his willingness to welcome me next year, since 1 July 1975. Hence, for the second time I had to pass on my *Via dolorosa* in Varna and Sofia. Meaning I received *NO* in quadruplicate, three *NO* from my school and the fourth *NO* from the president of Medical Academy, a totalitarian master in writing big-sized letters.

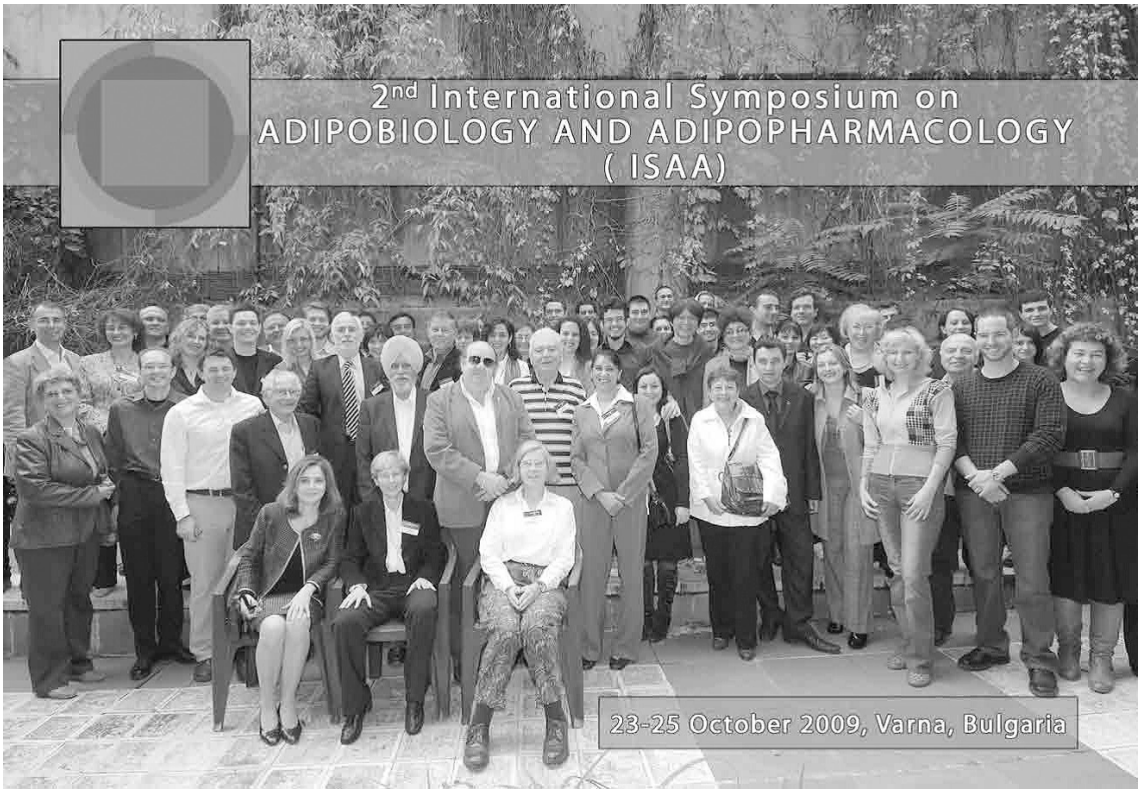
1973-NOW: RESEARCH-AND-TEACHING COUPLING

Excitation-contraction coupling (in muscle cells) and stimulus-secretion coupling (in secretory cell types) are known phenomena in cell biology. When we dubbed a subtype of SMC "secretory-contractile", we proposed the term "double coupling" believing that these SMC are capable of performing both contraction-relaxation and secretion (*Adv Exp Med Biol* 1975; 57:14–20).

Since July 1970, for some 3-4 years, I was research associate at Laboratory of Electron Microscopy – research only, no teaching. Later was appointed Assistant Professor at Department of Anatomy and Histology, and in 1987 elected Associate Professor in Histology and Head of Laboratory of Electron Microscopy. In my native country Bulgaria, I have never been promoted to Full Professor, whereas being elected Guest Professor in 3 universities and *Doctor Honoris Causa* in one university abroad. And having among the highest publication activity in Bulgarian biomedical community - impact factor over 190, citation index over 500, criteria having no priority in the habilitation in Bulgaria.

Whatsoever, since the academic year 1973-1974 it has been given to me *ius docendi* (Latin - right of teaching) medical students in histology and cytology. That time, even now, the official medical eduction system in Bulgaria does not appreciate cell biology in its curricula. However, my friends and I did our very best to escape from such an anachronism.

1 Although he as well as other commie leaders did explore all the benefits of western countries. Also nowadays during the democratic changes in Bulgaria, when their political power was transdifferentiated into financial power, not without western collaboration. This later process provoked me to write an essay entitled "Programmed disappointment from democracy" recently released in electronic newspapers only. Because there is a censorship in many, if not all, printed newspapers and magazines, also documented by international institutions. Despite all such disappointments, we, mostly educated Bulgarians, are appreciating today's democracy as compared to the previous, commie regime. In the last 22 years we are enjoying the freedom of moving, speaking, writing, and thus exploring our own intellectual potentials - even *in situ*, in our country, though the present administrations responsible for national health, education and science not yet support in priority the creativity and innovation, whereas preffering the commercialism. Despite of that, we know that during the commie regime in Bulgaria it would be not allowed to my friends and me to make Biomedical Forum, *Biomedical Reviews*, *Adipobiology*, ISAA, text book of Cell Biology, foundation of BGSCB as well as "George 50".



Noteworthy, immediately after the liberation from commie regime in November 1989, a chance for the upregulation of one's potentials also smiled to us, non-administrators but strongly devoted to research-and-education. Hence, since 1990 now, we, in collaboration with the respective university rector (for the first time democratically elected), have been organizing Biomedical Forum (BMF), a continuing medical education consisted of 8-10 lectures per academic year delivered by invited speakers from Bulgaria and abroad. That BMF is indeed a "continuing education" is proven by a post-lecture event, the liquid discussion (LD). It is processed in a restaurant near the university. Each LD is a get-together of the lector, organizers and 10-15, less or more, teachers and students.

In 1996, my *Textbook of Cell Biology* was released, and admired by students and teachers in Bulgarian medical universities (n=5) and biological faculties. In 2002, I proposed officially my laboratory to be renamed and that was accepted by the University Academic Board, thus Laboratory of Electron Microscopy became Division of Cell Biology.

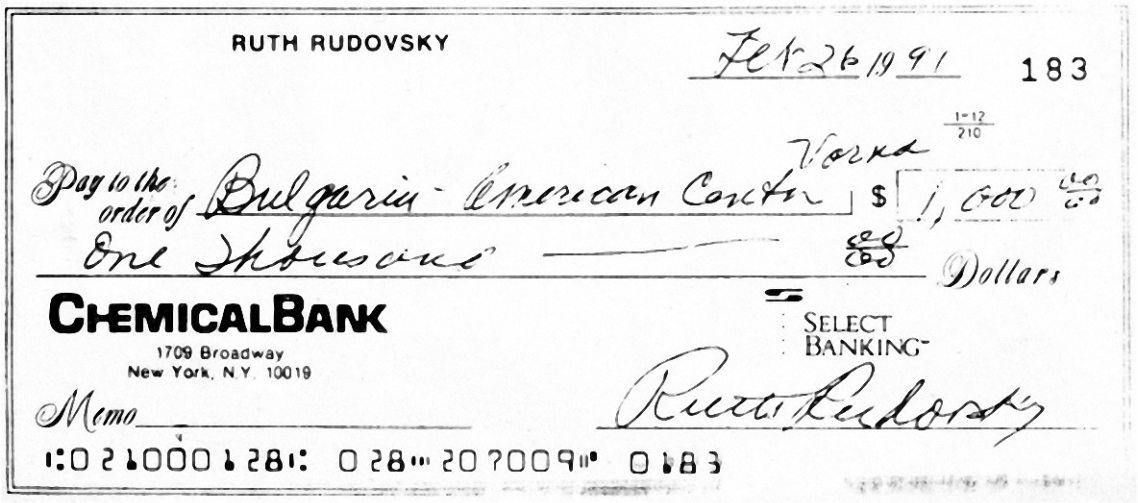
Pursuing our cell biology doctrine, in 2006 we founded the Bulgarian Society for Cell Biology (BGSCB), a professional society serving the cell biology community, promoting the advance of science, research and teaching. In 2009, BGSCB was elected a full member of the International Federation for Cell Biology (IFCB), as well as I was elected a member of the Editorial Board of *Cell Biology International*, a journal published on behalf of the IFCB. I would therefore like to express our cordial thanks to Professor Denys N. Wheatley, the President of IFCB and the Editor of *Cell Biology International*, for his support to our activities.

One more example of a creative and friendly togetherness is *Adipobiology*, an international journal for adipose tissue in health and disease, launched in 2009. As well as the organization of the International Symposia on Adipobiology and Adipopharmacology (ISAA), the 1st ISAA held in 2007 in Varna, the 2nd ISAA - 23-25 October 2009 in Varna, and the 3rd ISAA to be held 25-27 October 2012 in Burgas, Bulgaria.

1992-2012: BIRTH AND GROWTH OF *BMR*

Sometimes our best efforts do not go
amiss; sometimes we do as we meant to.
The sun will sometimes melt a field of sorrow
that seemed hard frozen: may it happen for you.
Sheenagh Pugh, *Somtimes*

The first volume of *Biomedical Reviews* (*BMR*), an international journal of cell biology of disease, was published in 1992. The Journal (ISSN 1314-1929) is published annually, and includes state-of-the-science Reviews and Dance Round articles (a form of short, position papers) focused on disease-oriented molecular cell biology, presented in concise form. The publication of *BMR* 1, 1992 was in a large part supported by the cheque of thousand US Dollars we received on behalf of Mrs Ruth Rudovsky. In the summer of 1990, we personally met in Varna with Mrs Rudovsky, a retired teacher from USA, on her tour in East European countries welcoming the democracy since 1989.


RUTH RUDOVSKY

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Memo

Ruth Rudovsky

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In 2011, we, Bulgarians, celebrated 22 years of democratic changes in our country. Coincidentally, BMR, volume 22 was released in the same year. Now we wish to cordially acknowledged the collaborative spirit and action of the generous Mrs Ruth Rudovsky.

On this platform, I want to also express our sincere appreciations to those who have volunteered to devote time and creative efforts, bringing their experience in learning and doing science to help guide the activity of BGSCB, including in-house and external peer-reviewing of the manuscript submitted to *BMR* published on behalf of the Bulgarian-American Center (1992-2006) and later by BGSCB (www.bgscb.org/BMR.htm). I serve as Editor-in-chief.

In 1992, Editor's Foreword of BMR, volume 1, started with the above cited poetry of Sheenagh Pugh, a British poet and novelist. Then, from London, I wrote: "After 45 years of sorrow, the "sometimes" melting point reached Bulgaria too. The Journal is a part of such a sometime-ness that has become possible through collaborative work with my friends, Dr Peter Ghenev, Dr Krikor Dikranian and Mr Krassen Kralev, executive director of the Bulgarian-American Center in Varna."

EFFECTS OF RESEARCH-AND-TEACHING COUPLING

In muscle cells, the excitation leads to contraction, whereas in secretory cells, the stimulus leads to discharge of exportable proteins. Whereas the research-and-teaching coupling has to produce both excellent studies and excellent students.

I have been trying to pleasantly apply such a "double coupling" to my students and research associates, also experimental animals and cultured cells. As I was taught from my parents, teachers and friends, at least three key messages are imprinted in-depth of my mind. First: the research needs both *Mens et Manus* (mind and hand), also the motto of Massachusetts Institute of Technology (MIT), Cambridge, MA. Second: "To study without thinking is nonsense. To think without studying is dangerous" – Confucius' advice. Third: *Aut viam inveniam aut faciam* (I will either find a way, or make one).

I have been conveying these messages to my students, some of them joined my lab in their first years of education, until the graduation. I repeatedly say to them: "One has to be courageous and lucky to at least a time cross at red light the main street of science, to make his own green path in biomedical research. Please, force your brain microscopes to escape the technical unsufficiency we, Bulgarians, are placed in our laboratories." Then, I tell my students a part of Robert Frost's *The road not taken:*

Two roads diverged in a yellow wood,
And sorry I could not travel both
I took the one less traveled by,
And that has made all the difference.

And my own writing titled *Homo liber*:

The individual freedom
You have to gain yourselves.
To follow the direction of your own compass,
To stay eye-to-eye with Hic sund leones [1]
To enter into terra incognita*,*
And say Eureka!
Like "two million cocks which broke the sky into pieces",[2]
To break the status quo.
"To live and let live",
But before anything
To learn the algorithm of tit-for-tat*,*
A reciprocal altruism -
The golden rule of human interactome.
The individual freedom
You may achieve it sometime –
See the snail is already reached the pick of mount Fuji.[3]

Fortunately, my students listened to me and most of them established a prestigious career in universities and hospitals of advanced countries. Their names, fields and coun-

1 Latin, "here are the lions", a warning note written by ancient Roman on the map to indicate a dangerous territory.

2 From Federico Garcia Lorca's ''Poet in New York''.

3 From a haiku by Kobayashi Issa:

O snail
Climb Mount Fuji,
But slowly, slowly!

tries they work are listed below chronologically:

1. Peter I. Ghenev, MD, PhD joined my laboratory in October 1973 when was first-year student. During 5-6 years of his medical eduction, he worked devotedly and precisely in the ultrastructure of vascular SMC – since then now we are friends and coworkers. In 1995 I invited Pofessor Christos Stournaras, Head of Biochemisty Department, Medical School in Heraklion, Crete, Greece, to lecture at BMF in Varna. Next year for 3-4 months Peter joined Stournaras' laboratory and studied heat shock proteins in cultured SMC. I was a supervisor of his PhD work he defended successfully in 2002. Now he is Associate Professor of Pathology and Head of Department of General and Clinical Pathology at our university. In 2004 I recommended Peter to the brilliant Hiroshi (Hiro) Yamamoto, Head of Department of Biochemistry and Molecular Vascular Biology at University Graduate School of Medical Science in Kanazawa, Japan, for 6 months. In 2008 he reduplicated his Japanese experience in Seiji Yano's Department of Medical Oncology in Kanazawa. "Kanazawa" literally means „marsh of gold"; sometimes you can even drink *sake* (rice wine) decorated with small pieces of gold.

2. Tanya Tenkova, MD was involved in eye research using TEM observations, and I supervised her work. In 1988 I recommended her to other brilliant Japanese friends, Shigeo Tsukahara, Head of Ophthalmology Department at Yamanashi Medical College in Tamaho, Yamanashi, and Takashi Fidjiwara at Anatomy Department, Medical School in Shigenobu, Ehime – she worked 6 months there. In 1992 Tanya won a USA fellowship and started to work in eye research in Medical School, Washington University (WASH U) in St Louis, MO. Since then now she is working there, married Professor John E. Heuser, a leading scientist (and artist) in cell biology, and thus made the biggest Bulgarian contribution to the world cell biology.

3. Krikor Dikranian, MD, PhD in 1995 won a position of visiting research fellow at Department of Anatomy and Neurobiology at WASH U. He produced exciting immunochemical and TEM micrographs from the brain of transgenic mice with Alzheimer's disease. Recently, Krikor was elected Associate Professor of Anatomy and Neurobiology. He was for several times rating the best teacher at WASH U. He is a member of the "Dream Team" of Dr David van Essen, the supervisor of the Human Connectome Project headquartered in their department. In our country, we essentially need such "dreams" to in priority be achieved and much later gold medals in Olympic games. *A fortiori*, "the world looks so different after learning science", quoting Richard Feynman, 1965 Nobelist in physics.

4. William Moreno Barrero, MD was our favorite Colombian student, his mother sent him in 1980 from Bogota to Varna via FedEx courier, to join my lab in 1981 when was second-year student. Among the first stories he told me was that the motto of Bogota is "2600 meters closer to the stars" but when he is there it is "2601 meters and 65 centimeters closer to the stars" – because I am 1.65 meters in height, he said. William used metaphoric expressions frequently in our everyday talks. Once upon a time of LD in Burgas, I told "William, your metaphoric language reminds me that of Gabriel Garcia Marquez." He replied: "All Colombians are at least second cousins of Gabo."

William applied his metaphorical imagination also in our research with rats and rabbits. Using TEM, he observed coated vesicles and receptosomes in SMC (*Acta Morphol Hung* 1986;34: 225-230), presented his observations at National Student Scientific Conference in Sofia, and won gold metal and diploma for his work. When his mother Donna Rossa arrived in Varna, he gave the medal and diploma to her. She was very proud of that and brought them to their house in Bogota. This will not be the only gold medal and

diploma in William's life. He graduated in 1986, we sent him to Colombia via FedEx courier, and Bogota became 2601 m and 65 cm closer to the stars again. At present, Dr William Moreno Barrero is one of the best phlebologists in Bogota. The diploma and medal are now on the wall of his office, and patients are also proud of their doctor's achievements.

5. Kamen Valchanov, MD joined my lab in 1992 when was second-year student. In 1994 and 1995, he attended international symposia in Oxford, UK and Eshişehir, Turkey, respectively. He graduated *summa cum laude* in December 1995 and in January 1996 flew to Department of Oral Biology at King's College in London, UK, to work on mast cells with Dr Gordon Proctor. Later he was trained in anesthesiology, and last 7-8 years Kamen is Consultant of Anesthesiology in Papworth Hospital, Cambridge, UK. An excellent example of filling the bench-to-bed gap.

6. Olawale A.R. Sulaiman, MD, PhD joined my lab in 1993 when was third-year student. In 1996 he attended Alzheimer's Disease School in Amsterdam, The Netherlands. In 1997 I invited Dr Ronald Mathison from Faculty of Medicine in Calgary, Alberta, Canada to lecture at Biomedical Forum in Varna. Ron presented a state-of-the-science lecture entitled "Would-be-worlds of salivary glands in inflammation", we had the traditional liquid discussion, I recommended Wale to work for him in Canada. And Wale flew to Calgary in the Fall of 1997, worked with Ron, later Ron sent Wale to Winnipeg, Manitoba, Canada to work on a PhD Thesis in neuroscience he defended excellently, married the charming Patricia enriching their family with 3 kids, moved to the USA, trained in neurosurgery, and last year elected Head of Department of Neurosurgery at Ochsner Foundation Hospital in New Orleans, LA. To certainly meet with Jack P. Strong, my "missed" Host Scientist – a phenomenon I formulate "the larger the brain-and-heart, the smaller the world". When was student, Wale's dream was to firstly work on PhD Thesis in neuroscience and then become neurosurgeon. His dream was materialized. This is a delight and honor for me. And for Emily Dickinson's *To Make a Prairie*.

7. Anton B. Tonchev, MD, PhD, DSc was born in 1973, just in the year when Peter Ghenev (presented above as my first university child) joined my lab. In 1992, Anton, a first-year student, appeared in my lab and asked me to be involved in my school of research. He worked insightfully, devotedly and precisely until 1998 when he graduated *summa cum laude*. Then I sent him to Dr Tetsumori Yamashima's Neuroscience Division at Department of Neurosurgery in Kanazawa. Anton worked 4 years there. Because he produced and published conceptually new (and beautiful) findings in a primate model of acute brain ischemia, Dr Yamashima asked me to send one more Bulgarian to his lab. This became a cascade event, thus the presence of Bulgarians in Kanazawa increased progressively since Anton's first shot (remembering of "hole-in-one" in golf). Hence Kanazawa became ideed a "marsh of gold" for many talented Bulgarians. Now Anton is Head of Department of Anatomy, Histology and Embryology at our university, and soon will be elected Professor.

8. Ralitsa Petrova, MD – in 2000 Anton and I recommended her to Hiro Yamamoto in Kanazawa. Ralitsa spent two years there, produced two papers on advanced glycation endproducts (AGE) and receptor for AGE (RAGE) in diabetes-related cardiac dysfunction, fallen in love with one Burgas-born young man she met in Japan, both returned home, married, and she became Ralitsa Chavdarova. Now Dr Chavdarova is a renowned cardiologist in Burgas.

9. Boryana K. Popivanova, MD, PhD – in 2002 I recommend her to Professor Naofumi Mukaida and she joined his Division of Molecular Bioregulation at Cancer Research Institute in Kanazawa. She published exciting results about the involvement of CCL2,

cyclooxygenase-2, and TNF-α in colorectal carcinogenesis in experimental models, defending successfully her PhD work. At present, Boryana is continuing her research in Keio University in Tokyo.

10. Galina V. Marinova MD, PhD joined my lab in 1996 when was second-year student. In 2002 she won a fellowship for PhD Thesis on the role of NO, NOS and arginase in vasculogenic erectile dysfunction. Galya worked in Department of Reproductive Medicine at Medical and Dental University in Tokyo, spent 4 years in Japan, defended here PhD successfully, and then moved directly to Dresden, Germany, to be trained in obstetrics and gynecology, and married a colleague who also graduated from our institute and used to work in Japan.

11. Juliya Yosifova, MD, PhD - in 1996 when was second-year student she joined my lab very enthusiastically, until her graduation. During this period of time, Yuliya was strictly supervised by her grandmother – as a results of that she attended 2-3 student scientific symposia. In 2002 Yuliya won a fellowship for PhD Thesis in immunology in University of Cincinnati, Cincinnati, Ohio, defended it successfully, married in the USA, and now is Chief Expert in Centers for Disease Control and Prevention, in Atlanta, Georgia.

12. Desislav Kaplamadzhiev, MD, PhD – in 2006 Anton and I "submitted" him to Tetsumori Yamashima's Neuroscience Laboratory in Kanazawa, where he did excellently his PhD work on neuronal stem cells. Spending 3-4 years in Japan, now, in a hospital in Sofia, Desislav is executing his dream to be a cardiovascular surgeon.

13. Danko Georgiev, MD, PhD joined my lab in 1999 when was second-year student. In 2005 I recommended Danko to Yukio Yoneda sen-sei, and he joined his Department of Pharmacology in Kanazawa. His brilliant brain produced novel data for the role of NMDA receptors in neuronal differentiation, the topic of his PhD Thesis. Since 2008 he is a Post Doctoral Fellow at Department of Psychiatry and Neurobiology in Kanazawa continuing his research on molecular aspects of schizophrenia, also in collaboration with University Departments of Neuroscience and Psychiatry in Pittsburgh, PA, USA (PLoS One 2012; 7: e43904). Along these studies, Danko is renowned in the filed of dynamic timescale of mind-brain interaction and quantum mechanics in consciousness, particularly the significance of neuronal microtubules in this multiplex phenomenon.

14. Ivan S. Donev, MD, PhD – in 2007 Anton and I recommended him to Seiji Yano's Medical Oncology Department in Kanazawa, where defended successfully his PhD Thesis on the development of novel pharmacotherapeutic approaches for treatment of lung cancer targeting HGF and EGF receptor pathways, a recent paper published in *Am J Pathol* 2012;181:1034-1043. In 2012, he delivered his back-home lecture at BMF in Varna. Now Ivan is working in Department of Medical Oncology headed by Dimitar Kalev, MD, PhD, our *summa cum laude* graduate, renowned expert in pulmology, laboratory medicine and philosophical poetry, a cluster leading to our BHF.

15. Nadezhda B. Boneva, MD, PhD - in 2007 Anton and I recommended her to Yamashima's in Kanazawa, where defended successfully her PhD Thesis on fatty acid-binding proteins (FABP) and G protein-coupled receptor 40 (GPR40) in neurogenesis in the adult primate hippocampus. In 2011, she delivered her back-home lecture at BMF in Varna. Now Nadya is training in neurology in the university hospital in Varna.

16. Dimitar D. Kostov, MD studied medicine during the academic years 1996-2002. Rarely entering my lab, he was a frequenter at BMF, hence *piano, piano* (Italian - slowly, slowly) we became BHF and later BHM that will be disclosed below in the text. In 2007 I recommended Dimitar to my former host scientist Yukio Yamori, and he obtained a grant from Matsumae International Foundation, for 6 months in Mukogawa Women's University

in Nishinomiya, near Kyoto. He studied the role of periadventitial adipose tissue (PAAT) in the contraction-relaxation activity of aorta, as a potential path in hypertensogenesis. More importantly, he met there a charming and bright Kanta Chechi, an Indian PhD student in Memorial University in St John's, Newfoundland, Canada. She also was a visiting fellow in Yamori's lab. Kanta and Dimitar fallen in love and a year later married. This was a very romantic issue of a cascade of the following friendly interactomics. In 2006 I was invited to lecture at the satellite atherosclerosis symposium in Belgrade, Serbia. I told the chairman, Professor Dragan Djuric, I cannot come because will attend the hub symposium in Rome. And proposed him to invite Dr Yamori. Dr Djuric invited Yamori, Kanta's supervisor Sukhinder Cheema also was in Belgrade met with Yamori, and thus Kanta appeared in his lab exactly when Dimitar was there – "adventures in Wonderland" of interactomics! Now Kanta and Dimitar enjoying their work and love in Quebec City in Canada. And we are now BHM, an Indian version of BHF, because "mitr" is "friend" in Indian.

17. Feodora I. Kostadinova, MD, PhD – in 2006 Anton and I recommended her to Naofumi Mukaida's Laboratory in Kanazawa. She defended successfully her PhD Thesis on the role of chemokine CX3CL1 (fractalkine) in inflammatory bowel disease, and directly moved to University of Konstanz, one of the elite universities in Germany; for further research work. In 2011, she delivered her back-home lecture at BMF in Varna and returned in Konstanz.

18. Rouzha Pancheva, MD, PhD – "you are so beautiful", as singing Joe Cocker. She joined my lab in 1993 when was third-year student. After her graduation, we decided to leave her in Varna to improve Bulgarian demographic status. Rouzha married and indeed contributed to the status delivering two boys and one girl. Now she is a university pediatrician in Varna, and renowned expert in breastfeeding.

I am also proud with my students who did not work in my lab but we became BHF during their education in Varna Medical University. I may write a book describing them, now mentioning only few of them.

Alexander I. Hinev MD, PhD, a *summa cum laude* graduate, now Associate Professor and Head of Urology Clinic at St Marina University Hospital in Varna, who - assisted by Dr Deyan Anakievski, Dr George Popov and Dr Chavdar Bachvarov - nephrectomised my left kidney on 22 October 2008, hopefully diagnosed renal adenoma (a benign kidney tumor), also confirmed by Japanese pathologists and Peter Ghenev who worked that time in Kanazawa. Afterward, our family doctors Pavlina Gherova and Andrey Zabunov touched my heart saying "You taught us about cells, now cells are thankful to you."

Kosta V. Kostov, MD, PhD, a native of Burgas, is also a *summa cum laude* graduate from our university. Due to his friendly and altruistic behavior, his nickname is Coro, coming from *cor* (Latin, heart). Now he is Associate Professor and Head of Pulmology Clinic at Military Medical Academy in Sofia, and Editor-in-chief of *InSpiro*, a unique quarterly. published science and art inspirations. Coro is a friend and co-singer of Ken Hensley, from the rock band *Uriah Heep*. Their song *July Morning*, became a motto of the Bulgarian tradition welcoming the sunrise on 1 July in cities along the whole Bulgarian Black Sea coast, originated in 1980 on south beach of Varna, a place closed to "Atmosphere Beach", a pub where my friends and I are meeting for lunch each second and fourth Saturday of a month, a tradition of Saturday Lunch initiated in 1990, sometime resounded with the melodies of Dr Kostov's saxophone.

Iliyan S. Ivanov, MD migrated in 1994 in Midwest USA and since 1997 working in Department of Adolescent and Pediatric Psychiatry at Mount Sinai School of Medicine in New York, NY. A native of Burgas, living in the heart of Manhattan, Iliyan is an example

of a Renaissance man, a creative cluster of psychiatrist, artist and musician, his "psychiatric" jazz group named "Shrinks" (Iliyan's website: www.rikka-arts.com).

So what - asked the brilliant jazzman Miles Davis. My answer is "I am very much proud of the achievements of my former students and present BHF."

The study of being a teacher, pedagogue (Greek, „to lead the child"; *paidos*, "child", *ago*, "lead") is among the most responsible human duties. Etymologically, in the word "education" there is also "to lead" (Latin, *ducere*) – to "bring forth what is within", "bring out potential" of your students. To lead them on the triarchy path of information, knowledge and way of thinking, including the moral sense in human interactomics – this "educational rhythm" (remember Alfred Whitehead's "The Aim of Education") is my philosophy in teaching students to *becoming* excellent physicians, scientists and, overall, human *being*. In effect, all of us, teachers and students, could understand that "the world looks so different after learning science *and teaching students*", paraphrasing Richard Feynman, the 1965 Nobel Prize-winning physicist.

In the context of pedagogy, I believe that teachers and students has to greet each other saying *sciavo* (Italian, will serve you), a lesson from the ancient people of Venice. (Much later, *sciavo* modulated into *ciao*, today's Italian most popular greeting.) Then, some of your students may call you "Uncle George", "Father George", "Master", or "Magister meos", as Dr Marco Fiore call me.

That is my *magnum opus* indeed.

1976: IN BUDAPEST, THE BEST IN EAST

Once my efforts failed to move Westward, I reminded myself few of Nietzsche's aphorisms, for example, "Hope is the worst of all evils because it prolongs our suffers" and the countering one: "That which does not kill us makes us stronger." Preferring the latter, I turned my eyes to the best in Eastlands. For my research field that was the 2nd Department of Pathology, Semmelweis Medical University (Hungarian, Semmelweis Orvostudományi Egyetem - SOTE) in Budapest headed by Professor Harry Jellinek, whereas Professor Anna Kádár was Head of Electron Microscopy Laboratory - recommended by them, my fellowship was from the Hungarian Atherosclerosis Society.

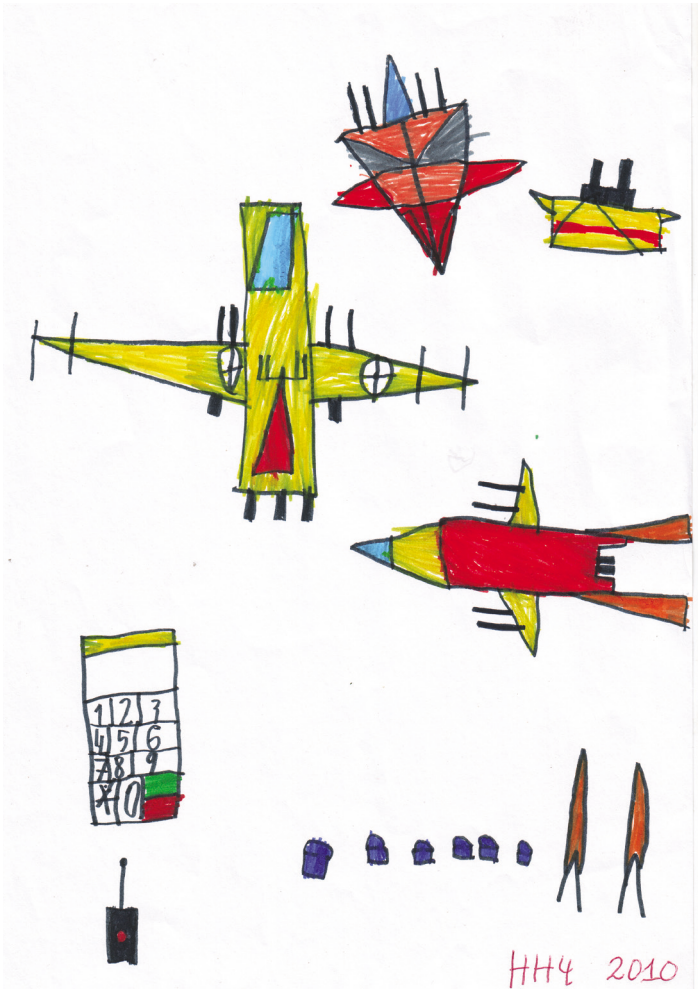
During the first days of my stay, Professor Jellinek invited me to lecture at a meeting of pathologists in Budapest. He introduced me with warm words, some of them were articulated as follows: "George Chaldakov for the first time linked cell secretion to vascular SMC, and since then these two entities fallen in a romantic love." Such a metaphoric expression about one's research touched my brain-and-heart indeed.

Using TEM, Dr Kádár and I studied vascular SMC, also in cultures treated with colchicines or lumicolchicine[1,2]. I spent 4 months in Budapest, a pleasurable time of work and friendship.

Later, in 1981 and 1982, I was also supported by Harry Jellinek and Anna Kádár and work 1-2 months in their department. Along with a laboratory work, I enjoyed friendly relations with them, also Dr Tibor Kerényi, Dr Eva Chonka, Professor Koch, Zsike, a

1 Kádár A, Csonka E, Veress B, Chaldakov G, Bihari-Varga M. Ultrastructural and functional aspects of vascular smooth muscle cells. *Prog Biochem Pharmacol* 1977; 13: 84-87.

2 Chaldakov GN, Kádár A. Microtubules in arterial smooth muscle cells in vivo and in tissue culture. An electron microscope study. In: W. Hauss, R. Wissler, R. Lehman, editors. *State of Prevention and Therapy of Human Arteriosclerosis and in Animal Models.* Rheinisch-Westfalische Akad. Der Wissenschaften, 1978, p. 211-231.



Sky's Smiles, *photograph by Nikifor N. Chaldakov (7), my grandson.*

technician, Zoltan, who is now Professor of Neurology, another Zoltan, a TEM technician, Vilma Kis, a PhD student, and Julia Kishegyi, a medical student - daughter of the famous opera tenor Arpad Kishegyi.

While in my 1980's visits I met with Vilma frequently because working in the same lab, during my 1976 visit in Budapest, I frequently met with Julia. She invited me to her house and introduced me to her parents. Strangely, the Hungarian State Opera House became the opera I visted as much frequently as no any other opera in the world. We usually sat in a royal box in the middle of first balcony. However, during our third visit, I expressed a somnolence-like behavior that was immediately recognized by Julia's receptors followed by a signal transduction that translocated us from the royal box to *Ballet Cipö* (Ballet Shoe) Bar, just behind the opera house. The bar, in fact, café restaurant, received its name in 1948 after its first owner, who was a ballet-lady. Afterward Julia no more invited me to Hungarian State Opera House, but frequently just-behind it. In my next visit in Budapest, I hope Julia will invite me to the Hungarian Institute of Cardiology where she is working now.

In 2010, on occasion of my 70th birthday, Anna Kádár sent me an e-message: "Dear George, I am glad you enjoyed your important anniversary. I am going to meet J.P. Stong in Washington in 3 weeks time. Any message for you? Yes, George, you are a survival, even more! You made a nice career with great achievements. Nice how you remember of us and the days so nicely you spent here. With warm greetings. Anna."

1977-1979: A SEVERE DEPRESSION I HAVE FALLEN

"Yes, George, … nice how you remember of us" as Anna Kádár wrote to me. Certainly, I can not forget my Hungarian friends because they saved me in a very critical period of my life. However, the salvage was temporal.

In the summer of 1977 I attended an international atherosclerosis meeting in Münster, West Germany, due a thanksgiving of Harry Jellinek and Anna Kádár, my new scientific parents. Around that period of time I started to feel I am melancholic, sleepless and various such symptoms of neuropsychological discomfort, a matter too strange,

never envisaged could be happened to my spontaneously vital personality that allowed me to insightfully work more than 12 hours daily, without forgetting *joie de vivre*. I have presented my lecture in Münster with seemingly the rest of my mental and emotional power. Returned home, I progressively fallen in a depression, lasting from the beginning of August 1977 to the end of September 1999. Two years in the jail of a severe depression – things happened around you but having neither mental, nor emotional power to reflect to them, nor to your memories. A reflectionless, powerlessness, helplessness resulting in *coer dolor* (heart pain) as described by French psychiatrists.

"It was only that and light was all it needed and a certain cleanness and order. Some lived in it and never felt it but he knew it all was *nada y pues nada y nada y pues nada*" (Spanish - nothingness and only nothingness…) - from *A Clean and Well-lighted Place* by Ernest Hemingway.

1983: ROCHESTER, MN AND CHICAGO, IL

In fact, the discovery of the Pill (I wrote about in *Lyuboznanie*) was a great invention where the role played by Gregory Goodwin Pincus was the great. Oscar Hechter, has written "Homage to Gregory Pincus" published in *Perspectives in Biology and Medicine,* Spring 1968; *In Memoriam* issue *to Gregory Pincus*). Oscar wrote: "I feel that Gregory Goodwin Pincus - Goody to his friends - is too big a man to treat in a ritualistic fashion. Pincus for me represents the prototype of a *new* scientist, whose life and achievements merit critical examination and analysis. Pincus and his life merit a critical case history, because if new Pincuses arise in the future, they will have a powerful impact upon the world."

In 1981, Oscar sent me a reprint of "The Homage", with a note on its first page: "To George, let our friendship progress. Oscar." Oscar Hechter was Professor and Head, Department of Physiology, Northwestern's School of Medicine, Chicago, IL. His steroid hormone research also contributed to the development of the Pill. For the first time we met each other during an international symposium in Varna in 1980 organized by the Bulgarian Academy of Sciences - a young lady, Professor of Biophysics, had good relations with commie leaders, thus having a chance to invite Western scientists including Nobel Laureates. In 1980, Oscar Hechter was one the most honored speakers at the symposium. We spontaneously get mutual understanding on both scientific and personal level. This certainly meant that we had to visit my native house in Burgas, 140 km south from Varna – my mother and my aunt were used to welcome my friends.

Since our meeting in Varna, we kept in touch by exchanging letters and research articles. Oscar, as he used to say, was "the brain of laboratory". In his post-steroid period of research he was a highly-tuned conceptualist, writing over 100 pages reviews on, for example, cyclic AMP's second messenger role in mediating hormonal effects (Hecther O, Halkerston IDK. On the action of mammalian hormones. In: *The Hormones*. Volume 5, Academic Press Inc., New York, 1964. pp 697-816).

In 1983, I was supported by the International Union of Angiology and the Mayo Foundation to present both lecture and poster at the 13th World Angiology Congress held in Rochester, MN. My Host Scientist was Dr Alexander Schirger, a renowned cardiologist at Mayo Clinic, and President of the Congress. For me, Rochester, MN became a paradise city of Drs Mayo, father and two sons - very safe, very clean, people exchanged greetings each other on the street, doors of houses and cars not lucked. Alex and colleagues did organize an excellent event at both scientific and social level. During these 5-6 days

in Rochester, each evening he invited a group of 25-30 participants per party - Alex never forgot me. Since then we became friends including with the members of his family, especially his son John – that time a boy, now cardiologist at Mayo Medical School. Even, in the beginning of 21st century Alex invited me to work as visiting research fellow at Mayo Medical School. I wrote him: "Thank you, I will come next century." Because his invitation followed that I have been received from Medical School in Kanazawa, Japan. Of note, David G. Holmes, a hospital sales representative of CIBA-GEIGY, was also very friendly to me, he invited me for lunch and dinner in his family house.

From Rochester I went for 4-5 days in Chicago, IL, where my Host Scientist was George Pappas, Professor and Head, Department of Anatomy, University of Chicago. I have introduced George to Oscar Hechter. They both invited me at their homes for lunch and dinner. We also visited 3-4 pubs, and the sky bar of Sears Tower (since 2009 renamed Willis Tower), also its observation deck (the skydeck) located on the 103rd floor at 412 m - from where I felt just approaching the heart of Chicago's sky.

George Pappas organized a seminar lecture, my talk was about secretory state SMC, in essence, the same lecture I have presented in Rochester. Forgot, in Rochester not in Chicago, a journalist interviewed me, and later published the interview in *Cardiology Today*, a monthly newspaper for cardiologists.

1985: RESEARCH FELOW IN PRAGUE, CZECHOSLOVAKIA

Professor Zdeněk Deyl at the Institute of Physiology of Chechoslovak Academy of Sciences invited and supported me twice for a couple of weeks in Prague. Reciprocally he visited my lab and delivered his SOS lecture. We easily got a mutual understanding at both professional and personal level. Zdeněk was a great man, perfect biochemist and master in chromatographic analyses. Both in Prague and Varna we enjoyed many LD, *U Fleků* (Czech, "At Fleků") being my *axis mundi* of Prague, since 1965 when, as a student on the route to conference in Poland, for the first time visited this brewery and restaurant built in 1499. In effect, we published 2 common articles [1,2].

1985, 1986: RESEARCH FELLOW IN MŰNSER, WEST GERMANY

Professor W.H. Hauss was a famous cardiologist and the founder of the Institute for Arteriosclerosis Research at the University of Münster, West Germany. He was my Host Scientist twice for 2-3 months in 1985 and 1986, also 1977 for the Münster International Arteriosclerosis Symposium. I used to work with Dr Jöerg Grüenwald, a young and very dynamic man, even a bit or more playboy or hippie, particularly the latter led to 2 common publications [3,4]. Later, I invited Jöerg and he presented a special talk in Varna.

1 . Deyl Z, Jelinek J, Macek K, Chaldakov G, Vankov VN. Collagen and elastin in the aorta of spontaneously hypertensive rats. *Blood Vessels* 1987; 24: 313-320.

2 Chaldakov GN, Deyl Z, Vankov VN. Colchicine: possible new application of its antifibrotic (antisecretory) action.[mini-review]. *Physiol Bohemoslov* 1987; 36: 1-7.

3 Chaldakov GN, Grüenwald J. Effect of colchicine on the ultrastructure of secretory-state smooth muscle cells from the rabbit artery wall. *Exp Pathol* 1987; 31:1-9.

4 Grüenwald J, Chaldakov GN, Haudenschil CC. The effect of calcium antagonists in experimental atherosclerosis, the underlying cause of heart and cerebral vascular diseases. In: Hartman A, Wkushinky B, editors. *Cerebral Ischemia and Calcium*. Springer Verlag, Berlin. 1988; 201-212.

1986: RESEARCH FELOW IN TŰBINGEN, WEST GERMANY

I worked one month in Cell Culture Laboratory of Department of Physiology in Tübingen, West Germany, headed by Professor Betz, a nobleman. With one of his young coworker we treated cultured vascular SMC with verapamil, a calcium blocker, and observed structural alterations. When the SMC went to sleep, I finalized our review article on the secretion in SMC with special reference to Golgi complex and microtubules, submitted the manuscript to *Atherosclerosis*, it passed successfully through peer-reviewers, revision and resubmission, thus released in the same year 1986. To more respectfully be introduced by my Host Scientist before my inaugural lecture in Izumo, Japan.

1986-1987: RESEARCH FELLOW IN IZUMO, JAPAN

Since the Heidelberg-1973 symposium, in 1982 it was my second appearance at symposia organized by the International Atherosclerosis Society (IAS). The symposium was in West Berlin, Germany. Thanks to my international scientific parents, I was already a less-or-more recognized member in vascular biology community. Consequently, I was invited by the Organizers to serve as a discussant of a session on SMC in atherogenesis. My duty was to make a sum-up of the presented lectures and conduct the discussion. One of the speakers was Professor Yukio Yamori, Head of Department of Pathology and Director of the Japan Stroke Prevention Center, Shimane Medical University in Izumo, Japan. Perhaps, due to such a “superior” position I was granted, he first approached me and we started to discuss. Prospectively, we became friends, *tomodachi* in Japanese. A really good news I obtained from Japan found me in Tübingen-1986, just before my transmigration to Münster – Yamori *sensei* arranged a fellowship for me from the Japan Society for the Promotion of Science (JSPS), for 7 months from October 1986.

Sensei is a Japanese word which literally translated means “person born before another”, used as “teacher”, “Master”, a respectful title for teachers, physicians, lawyers and famous writers and artists, whereas for others is “san”, both for men and women. Likewise, Japan is Nippon or Nihon, usually translated “The land of the rising sun”, while my translation is “The land of sun’s roots”.

I arrived at Tokyo Narita airport on 1 October 1986, Yamori sensei welcomed me, we flew to Osaka, spending there and in Kyoto 2-3 wonderful days before flying to Izumo. In the garden of Kyoto’s temple, Dr Yamori gifted me a medallion with a hole shaped like square in the middle, around which was written with kanji (old Chinese characters used in Japan): “I know satisfaction only” (forget Rolling Stones’ “I can’t get no satisfaction”). The Japanese “satisfaction” transmits a great meaning: one should get satisfaction from everything doing. And not aim at tasks which cannot achieve, because will get frustration, instead satisfaction. I call this “wisdom of satisfaction”.

However, only few of many Japaneses I asked could read “I know satisfaction only” written with their own characters. Yamori sensei was among these “few Japaneses”, because he as well as some other sensei I met (Yasuo Uehara and Takashi Fujiwara in Sigenobu, Shigeo Tsukahara in Tamaho, Hiro Yamamoto, Yoh Takuwa and Shinichi Harada in Kanazawa) know more than 10 000 kanji, whereas an university graduate knows about 3 500 kanji. Nonetheless, many, if not all, Japanese follow this message in their everyday life. Most probably here is stemmed an important component of Japanese’s way of thinking and lifestyle.

Another such component could be found in *Roanji Garden* in Kyoto where 15 stones

are arranged in a pattern one can see 14 of them only whatsoever position is taken for his/her obesrvation. That is, one should change the observational loci to get whole view of the exposome (surrounding world). Though, the “The Holly elephant had a hundred names, the real one being the hundred and first, known only to the elephant himself” - said by the great Albert Szent-Györgyi in his special talk “Retrospect and Apology” presented at a symposium of the American Association of Muscular Dystrophy and published in: Milhorat AT, editor. *Exploratory Concepts in Muscular Dystrophy and Related Disorders*. New York, Excerpta Medica Foundation, 1966; 112-114.

In Izumo I was accommodated in Guest House located in the university campus, the family of Tsutomu Adachi san taking care for the guests. I spent over 12 hours daily in the lab and whenever returned “home”, usually after midnight, Tsutomu welcomed me on the entrance door (reminding me my mother’s waiting for me) with a progress report saying in Japanese English “Today five guesto, you and other four”. Then we moved to the dining room, he took a single, I double Suntory whisky before exchanging “good night”. Only these latter words meant for Tsutomu that his working day is finished, and he went to sleep, leaving me to further meditate liquidly. Next morning, the breakfast prepared by Sanaya, Tsutomu’s wife, waited its guests. Obviously, I will never forget the family Adachi – Tsutomu, Sanaya and their two daughters, smiling in Japanese.

In the first week of my stay in Izumo, on occasion of 11th anniversary of Shimane Medical University, many cultural and funny events were organized in the campus. One of the events was a competition for Miss University. Alex and I were invited members of the jury, thus we also contributed to the selection of 3 beauty queens. At evening, group of students invited us to a party (in fact, Bulgarian LD) in a Japanese style restaurant followed by “a continuing education” in a cascade way, that is, a movement from one to another bar. In this overnight party we met with many students and teachers – one of them a charming Japanese lady who studied fine art. Later she showed me many art galleries in Izumo. From one of them I bought 4 pictures by a Japanese artist collectively titled “The four seasons of the year” - since then now, they are enjoying us and the guests of our home in Varna. Listening Vivaldi’s “The four seasons” played by Nigel Kennedy, *The Seasons* look more beautiful. We also attended the jazz performance of Milcho Leviev (piano), a Bulgarian who migrated to USA in 1970, and David Holland (contrabass), in Jim Hall in Izumo.

Alex, an Armenian colleague from Russia (then still USSR), was a visiting research fellow at Biochemsity Department. He was a very clever, very friendly person. However, after work in the lab, he preferred to stay in the guest house even during the weekend, whereas I explored these two days waking, shoping and drinking downtown Izumo. Hence, owners of shops, karaoke bars and art galleries understood that I am Bulgarian, not American - seeing a foreigner, Japaneses first asking “Are you American?” This is why when Alex visited a shop or karaoke bar, the owners asked him “Are you Bulgarian?”

In Izumo I studied cultured SMC from spontaneously hypertensive rats (SHR) compared to Wistar-Kyoto normotensive rats, using light microscopy and SEM. I worked together with Dr Toru Nabika, a very bright and friendly young man. Antoaneta, my wife, arrived in Japan in the beginning of April, just in the first days of *sakura* – cherry blossom, lasting about 15 days to remind Japanese that happiness is a beautiful but short-lasting event. I dubbed this pheomenon “wisdom of sakura”.

Dr Yamori told Antoaneta that she may be jealous to me only from SMC I fallen in love. Indeed, I was delighted of a chance to apply my first, Varna research love, pharmacology, to Japanese SMC. All chemicals I asked Yamori sensei to purchase arrived within 2-3

days in the lab – with an exception, Yamori did not agree to purchase nerve growth factor (NGF). He friendly said to me: “George, that is too much crazy!” Yet, what was crazy in Izumo-1986 became a reality in Rome-1998.

In Izumo, we treated luckily our SMC with isoproterenol, dibutyril cAMP or other agents increasing cAMP concentration, or with cytochalasin B, a disrupter of actin filaments. These treatments resulted in a stellation (arborization) of SMC, they looked like neurons. Perhaps, SMC have never been so beautiful as in Yamori’s lab in Izumo. The beauty being distroyed by phorbol 12-myristate 13-acetate as well as colchicine but not lumicolchicine treatment, suggesting the beauty required fresh PKC and MT, respectively [1,2].

Antoaneta and I visited Tokyo, Osaka, Kyoto, Shigenobu, also Hinomisaki, a small town located north of Izumo where fish is more than rice, and the lighthouse is 38.8m high - the highest of stone-build lighthouses in Asia. From the upper deck we enjoyed the unique image of sunset over the Sea of Japan. Anywhere in Japan, to mention Yukio Yamori’s name was as much respectful as mentioning Rita Levi-Montalcini’s name in Italy.

When returned home, my friends asked me what mainly impressed me in Japan. I replied: “In Japan one can see everything found in western countries, but in the western countries cannot see what found in Japan.” In other words, Japan is (still) a symbiosis of tradition and innovation, both expressed through *fuga-no-michi* (the way of elegance), as in Matsuo Basho’s finest haiku.

1987 IN SHIGENOBU: IN SEARCH FOR MORE BEAUTY

Before we met *in vivo*, I knew Yasuo Uehara *in libro* - his beautiful SEM micrographs of SMC, pericytes, nerves, neuromuscular junctions, the images excited my esthetic view in cell science. In my experience, other examples of such an emphatic view of cell structures are John Heuser’s micrographs obtained with his method of quick-freeze deep-etch TEM.

Professor Yasuo Uehara was Head of Department of Anatomy, Medical School in Shigenobu, Ehime prefecture on the island of Shikoku. I met with him for the first time after his lecture in Izumo; he was invited by Dr Yamori. The SEM micrographs shown in the lecture appeared even more beautiful for me than those published in the journals. This is why I immediately asked Dr Yamori to send me to Uehara’s lab to learn his SEM method of visualization of adventitial aspect of SMC and, possibly, associated perivascular nerves. By bus or train, you have to reach firstly Hiroshima and then take a boat for Ehime – for 2-3 hours you are enjoying Japanese mother nature of too many islands around.

Yasuo Uehara and Takashi Fujiwara, welcomed me at the harbor of Ehime. After 30-40 minutes drive by car we reached Shigenobu, a small beautiful town (since 2001 merged with another town and renamed Toon). During the first dinner Yasuo Uehara told me “Call me Yasuo.” Reciprocally, “Call me George” - I said to him. Articulated honestly, such an exchange of words is very meaningful, a promise for friendship delelopment. Here, in southern area of Japan, I met people expressing a warmer, Burgas-like behavior. Reminding me of cultural topology in the duality North-South. In my experience, it should not be the

1 Nabika T, Chaldakov GN, Nara Y, Endo J, Yamori Y. Phorbol 12-myristate 13-acetate prevents isoproterenol-induced morphological change in cultured vascular smooth muscle cells. *Exp Cell Res* 1988; 178: 358-368.

2 Chaldakov GN, Nabika T, Nara Y, Yamori Y. Cyclic AMP- and cytochalasin B-induced arborization in cultured aortic smooth muscle cells: its cytopharmacological characterization. *Cell Tissue Res* 1989; 255: 435-442.

physical distance that determines behavioral difference – distance Varna-Burgas is 140 km and Rome-Amantea is about 600 km, but southern people are more emotional, more open minded and, perhaps, more collaborative. This may also be the case for Izumo-Shigenobu and Kanazawa-Shigenobu. North or south, "I like more a good Japanese than a bad Bulgarian", paraphrising Federico Garcia Lorca's "I like more a good Chinese than a bad Spanish", a revitalization of Diogenes' cosmopolitan paradigm.

I liked very much to show the southern emotionality to my wife and we visited Yasuo's Shigenobu in the middle of April 1987, just in the season of *kaki* (Japanese Persimmon) - beautiful and tasteful fruits in size of apple and color of orange, when fully ripped, colored red. In a garden of *kaki* you may imagine you are in the Garden of Eden (Paradise). With a small difference only: *kaki* are not forbidden for eating. Because *kaki* is not Tree of knowledge, but Tree of beauty.

It was a hard and pleasant lab work in Shigenobu. Yasuo attached Takashi to me – he helped me very much in the development of a small, but effective, modification of Uehara's SEM method in visualizing the network of perivascular nerves – one more beauty, now in Shigenobu. We as well as other colleagues in the lab used to observe in TEM or SEM until late afternoon. In the same time, a Chinese colleague prepared the dinner in lab's kitchen. When the table for 10-12 persons was arranged, Yasuo started to call all of us articulating "It's time to fix our brains!" That is, sake, beer and whisky were also on the table. Like in Bulgaria, such dinners have no fixed closing time but always keeping in mind my father's message WHAT DID I ARRIVE HERE FOR?

From Yasuo and Takashi I learned a lot in SEM as well as the art of beauty. We, at Izumo, acknowledged their collaboration, but that was not enough for me – I did no success to motivate my Izumo's host scientist to agree Uehara and Fijiwara to be coauthors of our papers [1,2]. Sorry, Yasuo and Takashi!

1991: GUEST OF DR COSTANTINI'S HOUSE IN FREIBURG

In the fisrt months of Bulgarian democracy, on 23 February 1990, during the party for my 50th birth day, my friends and I, all dreamers for USA (that time), initiated the foundation of the Society of Friends of USA later renamed Bulgarian-American Center. A month later at the founding meeting I was elected Chairman of the Society. In the autumn of 1990, we invited our first official guest Dr Antonio Vito Costantini, USA-born Italian who knew only few Italian *parole* (words), an expert of high rank in internal medicine and ton rich several owner of clinics along the bay of San Francisco, CA. Because of his renewal insight in the pathogenesis and therapy of atherosclerosis, Dr Costantini contacted me in 1989. He was interested in our colchicine experiments in vascular SMC published in *Atherosclerosis* in 1982 and 1986. It was known that the antimitotic and antifungal drug griseofulvin is a potent microtubule-disassembling agent. Few papers also reported that griseofulvin suppresses angina pectoris. These data also triggered Dr Costantini's pursuit to Bulgaria. For the first time we however met each other in Vienna, Austria during a symposium of the European Atherosclerosis Society (EAS)

1 Chaldakov GN, Nara Y, Horie R, Yamori Y. A simple and reliable method for visualization of arterial autonomic nerve plexus by scanning electron microscopy. *Acta Morphol Neerl Scand* 1987; 25: 273-277.

2 Chaldakov GN, Nara Y, Horie R, Yamori Y. A new view of the arterial smooth muscle cells and autonomic nerve plexus by scanning electron microscopy in spontaneously hypertensive rats. *Exp Pathol* 1989; 36: 181-184.

held in the spring of 1989, I was invited and supported by the EAS. He presented his concept of fungalbionics of disease. Aged 65 years Dr Costantini was very enthusiastic about the role of fungi and micotoxins in atherosclerosis, gout (podagra), cancer and other lifestyle-related diseases. He believed it is not high-fat diet but the consumption of fungal fermentation foods (bread, cheese, beer, wine) places humans at potential risk of these diseases. I told him I appreciate his efforts, but fungalbionics is not my research field. So, he liked to introduce him to my colleague-friends around Vienna and we visited Dr Attila Czirfusz, a pharmacologist in Bratislava, Slovakia, and Dr Anna Kadar, a pathologist in Budapest, Hungary.

Toni was even more enthusiastic than me in the emerging democratic changes in Bulgaria, whereas we still worried about eventual commie repressions. Then in Vienna, Toni told me "George, I am your bodyguard in Bulgaria". This is why we invited Dr Antonio Vito Costantini as our first guest at a meeting of the Friends of USA Society in Varna. Moreover, he presented his fungalbionics lecture at BMF.

We became BHF with Toni. In 1991 I was invited to present a talk to Goethe University Medical School in Frankfurt, Germany, and Toni invited me to visit his big house in Freiburg. He lived with his second wife Ziggi, a charming German lady, some 15 years younger than Toni. And with their 4 kids – Tonya, Anton, Johan and Sebastian, now all over 30 years of age. I spent a nice week in the big house, everythings being at my disposal – "except Ziggi", Toni said to me. Certainly, it was easy for me because I am well trained to keep Command 7 of the Ten Commandments in Christian Decalogue, my wife doubts about that.

1991-1992: RESEARCH FELLOW IN LONDON, UK

Due to the recommendations of Professor Geoffrey Burnstock (we knew each other since Heidelberg-1973), a great scientist at the University College London (UCL), and of Dr Timothy Cohen at the Department of Anatomy and Developmental Biology, Royal Free Hospital School of Medicine (RFHSM) in London, UK, I won a fellowship for visiting research fellow from the Wellcome Trust, to work in Tim Cohen's lab for one year since October 1991. We, wife, son, his girlfriend, and I, rented an apartment house in the calm and artistic Hampstead region of London, near the school, *White Hours* and *The George*. My son Nikolai (Nick) and his girlfriend studied English, Nick also art photography.

At RFHSM I met with clever and friendly colleagues. I worked with Dr Tim Cohen, a very bright and polite person, and drank mainly with Tim Andrews and Chris Thrasivoulou, PhD students of Tim Sr, who was very enthusiastic in pursuing the primarily reason for age-related degeneration in perivascular nerves. Using TEM, every day I observed ultrathin sections from veins and cerebral arteries, and documented over thousand images of a beatiful degeneration in older SMC, a main source of neurotrophic signals, also counted the number of perivascular nerves and adventitial mast cells. For progess report, Tim and I visited Dr Burnstock at his lab in UCL once in 2-3 months to make a progress report. He enjoyed our results and prompted us to publish them. However, in a way I called "piece-by-piece", whereas I preferred to publish, for example, 2 "big" papers expressing our data of SMS and nerves/mast cells respectively, instead of 4-5 "small" papers. Amazingly, that time Dr Burnstock had over 900 publications in September 2012 reaching 1 187. Despite of that he extended my stay in London with 2 months, to finalize 2 "big" manuscripts, the results I previously presented to symposia

in Nottingham, UK and Lausanne, Switzerland [1,2]. I did my job and left the manuscripts to Geoffrey Burnstock and Tim Cohen. These were not transformed into articles in any journals until now. Thus I did not contribute to the progress of UK biomedical science. Though I have promised that to Burnstock. We took our coffee with Krikor Dikranian, my colleague-friend from Varna who worked that time for Burnstock in UCL. Burnstock entered the school bar and asked us “How is your research going?”. I replied “We are trying to improve UK science.”

1996: LECTURE IN ESKIŞEHIR, TURKEY

In 1992 I caught *in libro* that Professor Neşe Tunçel, Head of Department of Physiology at Osmangazi Unieversity in Eshişehir, Turkey, published interesting findings, and invited her to lecture at the BMF in Varna. One late evening of November 1992 she and husband, Professor Musaffer Tunçel, arrived in Varna. We moved to the University Guest House, enjoyed glasses of wine for weldrink, and next day Nese presented her VIP (vasoactive intestinal peptide) lecture followed by liquid and dancing discussion in the university bar. During 1990-2003, we enjoyed academic support of Professors Dimitar Kamburov and Temelko Temelkov, the first democratically elected rectors of our university.

Reciprocally, Dr Neşe Tunçel invited me and my wife to visit her university. One early evening of April 1996 we arrived in Istanbul welcomed by Neşe and Musafer. On the way to Eshişehir (Turkish, “old town”, about 400 km east from Istanbul) we visited two beautiful towns. In Eshişehir we were accommodated in the University Guest House. My lecture was scheduled for the next day. Coincidentally, Erdal İnönü from Ankara, Professor of Theoretical Physics and Prime Minister of Turkey (1991-1993), was invited to present his SOS lecture. He was accompanied by his guards and they all arrived the same day we were already in the Guest House. Guards checked the house, smiled friendly to us and took their strategic positions in and around the House. We accepted this as a respectful thrust to us, excluding the chance of being left as a target for an eventual attack over the former Turkish Prime Minister. The chance fortunately did not smile, and next day morning Erdal İnönü and I presented our lectures. Followed by a rich lunch attended by many university professors, Erdal İnönü, Neşe, Musaffer, my wife and I being placed centrally around the table. We had an academic and friendly talk. I remember that Professor İnönü admired our philosophy of BHF and shared its Turkish equivalent: “eline beynine saglik” (health for your brain and hand). Sounds like *Mens et Manus*, the motto of MIT, where Erdal İnönü used to deliver lectures. However, Neşe and Musafer were not in Cambridge, MA, to coincidentally invite me to lecture there.

Significantly, Neşe and Muzaffer (Zaffi) Tunçel became BHFF for me, my family and friends. They also introduced me to such bright and friendly Turkish colleagues as Professor Rümeysa Demirdamar, the Dean of Faculty of Pharmacy, Near East University in Nicosia, North Cyprus), Professor Levent Ozturk (Department of Physiology, Faculty of Medicine, Trakya University in Edirne) and the cahrming Fatma from University in Bolu and Bilge and Esin from Ankara University.

1 Chaldakov GN, Andrews T, Burnstock G, Cowen T. An ultrastructural study of aging in cerebral blood vessels: accumulation of neurofilaments and muscle basal lamina in old age. *Neurosci Lett* 1992; 42 (Suppl): S28.

2 Chaldakov GN, Andrews T, Burnstock G, Cowen T. An ultrastructural study of aging in perivascular nerves and mast cells of the rat. *J Neurol* 1992; 239 (Suppl 2): 127S.

1998-NOW: ROME, ITALY OR, STATE-OF-THE-DREAM

Some people are so much popular that it is enough to only abbreviate their names:
L – Carl Linnaeus
N – Napoleon Bonaparte
RDR – Franklin Delano Roosevelt
JFK – John Fitzgerald Kennedy
RLM – Rita Levi-Montalcini

As mentioned, during my student years in Varna I used to work 4 years (1962-1966) as research associate at the Department of Pharmacology. That time I for the first time met *in libro* Professor Rita Levi-Montalcini (RLM), reading her articles on nerve growth factor (NGF). Since then I have being infected by this talented molecule and searched how to reach her Institute in Rome, Italy. Although some colleagues told me that it is a very much difficult pursuit, I continued to believe in the art of dream as presented by Emily Dickinson's *To Make a Prairie* (*To make a prairie it takes a clover and one bee,/ One clover, and a bee,/And revery./ The dream alone will do,/ If bees are few.)*

In 1986-1987 (in Japan) I liked to study the effect of NGF on cultured SMC as well as in 1991-1992 (in England) the effect of NGF on mast cells of vascular wall (following Aloe and Levi-Montalcini's 1977 results of NGF-mast cell link). However, the host scientists have ignored my proposals. But not my Dream!

Hence, in 1995 I invited Dr Luigi Aloe, the long-lasting and most productive coworker of Levi-Montalcini, to lecture at both the Conference of Bulgarian Young Scientists and BMF 5 (1995-1996). The first days of October 1995 have just arrived in Varna, and the flight of Dr Aloe landed on Sofia airport with a delay, he missed the link to Varna, took a taxi (Sofia-Varna is about 6 hours drive), we welcomed him at late evening in the International House of Scientists, the venu of conference – it was just in the middle of cocktail when we started our first talks, first drinks. From psychoethology, it is known

that the first impressions are in-depth imprinted in one's mind (in sense of instinctive behavior described by 1973 Nobel laureate Konrad Lorenz). Something like that has happened both in Luigi's and my mind, a symptomatology promising a life-long BHF.

Next days Dr Aloe presented his two SOS on neuropsychoimmunology. He was awared by the Bulgarian Union of Scientists, the organizer of conference. I introduced Dr Aloe to my students, collectively named KARO (Kamen, Anton, Rouzha, Olawale). We spent together wonderful 3-4 days in Varna and Burgas.

In the beginning of 1998 I have applied for NATO-CNR Research Fellowship, which required acceptance letter by the host institution. My Dream asked Luigi Aloe about, he provided me such a letter, I was awarded the fellowship, and in June 1998 appeared in the Institute of Neurobiology, CNR, Rome, honorably chaired by RLM, a 1986 Nobel Prize winner for NGF discovery. I was pleased to ACAP (as creatively as possible) explore the chance to study the role of NGF in the pathogenesis of cardiometabolic diseases (atherosclerosis, obesity, type 2 diabetes, metabolic syndrome). Moreover, I was honored of having *in vivo* meetings with RLM. She invited Luigi and me several times to lunch and dinner at her house. In 1998 she gave me her book "The Saga of the Nerve Growth Factor" (released 1997) and wrote on an inside page: "To Dr George Chaldakov with friendship and warmest wishes. Rita Levi-Montalcini. 29 July 1998."

The road she traveled "from Turin to Stockholm via St. Louis and Rio de Janeiro" remains as a charismatic model for many generations pursuing their Dreams in research. That is what I call state-of-the-dream, one of the biggest shots in executing my maxim "from *in libro* to *in vivo* meetings" with famous scientists on our globe. When returned in Varna, I wrote an essay entitled "I met with Her Majesty RLM".

1998-NOW: SHUTTLING RESEARCH FELLOW IN ROME OR, *MIO ABC* LUIGI ALOE

In 1999 I nominated Dr Luigi Aloe for honorary degree of *Doctor Honoris Causa* of our University, and the Academic Board respectfully awarded him. That time Luigi arrived in Varna together with his charming daughter Silvia and his young coworkers Marco Fiore and Francesca Properzi, a collection of charming genes of Italy and Spain. She taught me how to say in Spanish *Verde que te quiero verde* (Green, how I want you green) from Federico Garcia Lorca's poem "Romance Sonambulo".

Francesco Angelucci was also included in Luigi's delegation. He explained to me that "vates" is Latin word for poet - it was believed that the poet is prophet, a man full with inspiration. During a coffee break in "La Mimosa" near the Institute, Francesco said to me: "Poetry is *una storia d'amore eternal*." He himself was a very artistic, Ovidian person. Even, he studied the effect of listening music (and poems) on brain levels of NGF and brain-derived neurotrophic factor (BDNF) in rats. Like another *amico Italiano*, Dr Enzo Emanuele at University Department of Psychiatry in Pavia, who aimed at the molecular dissection of the old adage "Love is a mistery". Enzo found that circulating NGF level, but not that of BDNF and other neurotrophins, was significantly increased in early-stage, intense romantic love and returned to basal level after the final of *storia d'amore acuta*, lasting 2-3 years only.

From Francesco I have also learned that for his *storia d'amore* Ovidius was exiled in Tomis, today's city of Constantza in Romania. This was happened during the time of Thracian tsar Cotis, who "certainly was one of the first poets in the region of Burgas' bay",

according to the 2011 book "The History of Burgas" authored by my friend Ivan Karayotov, Professor of Archeology.

Most probably I will write a special book about my meetings with Lugi Aloe and other *amici Italiani*, a 17-year-young story until now. I already published several Italian essays I already published in my 2010 book "The Human. Thoughts, Feelings, Friendship". The main heroes there are Luigi and Franca, his charming and noble wife, his son Gian-Luigi and grandson Federico. And signora Rosaria, Luigi's grandmother who is carefully watching whether we are drinking wine well enough to be closer to God, as she used to say. As well as Marco Fiore and his charming wife Caterina and their kids Spartaco and Manrico, Nicola Costa, Luigi Manni, Alessandro Lambiase, Sergio Bonini, Giovanni Nicotera, Salvatore Barba and *belle ragazze* Paola, Viviana, Federica, Valeria…

My position of shuttled research fellow (1998-now) have been supported by Italian institutions, particularly CNR. Reasonably enough to nickname Luigi Aloe *mio ABC* (*amico, banca e capo*) – my friend, bank and chief. As announced in the Dream, I arrived in Rome to study the possible involvement of the neurotrophins NGF and BDNF in the pathogenesis of cardiometabolic diseases, with a special focus on adipose tissue. It was hard, creative, pleasant lab work well coupled with *ad libitum* meal and wine. I was well trained in such a lifestyle in Bulgaria. Arguably, we obtained interesting, perhaps, new findings in human coronary atherosclerosis, metabolic syndrome, and acute coronary syndromes [1,2,3,4,5,6], summing them up in our 2011 metabotrophic article published in a special issue of *Arch Ital Biol* dedicated to 102nd Anniversary of RLM [7].

At adipobiological level, we have introduced the term adipokines in 2000 [8,9] to substitute "adipocytokines" not because it was a wrong term, but because considering adipocytes as the sole adipose source of these talented proteins (adipocyto-kines), or cytokines only as adipose-derived molecules (adipo-cytokines). Any related references before our publications in 2000 would be greatly appreciated.

1 Chaldakov GN, Fiore M, Stankulov IS, Hristova M, Angellini A, Manni L, Ghenev PI, Angelucci F, Aloe L. NGF, BDNF, leptin, and mast cells in human coronary atherosclerosis and metabolic syndrome. *Arch Physiol Biochem* 2001; 109: 357-360.

2 Chaldakov GN, Fiore M, Stankulov IS, Hristova M, Angellini A, Manni L, Ghenev PI, Angelucci F, Aloe L. Adipokines and neurotrophins in human cardiovascular and metabolic pathology: a new road ahead. *Scr Sci Med* 2001; 33: 101-104.

3 Chaldakov GN, Stankulov IS, Aloe L. Subepicardial adipose tissue in human coronary atherosclerosis: another neglected phenomenon. *Atherosclerosis* 2001; 154: 237-238.

4 Chaldakov GN, Stankulov IS, Fiore M, Ghenev PI, Aloe L. Nerve growth factor levels and mast cell distribution in human coronary atherosclerosis. *Atherosclerosis* 2001; 159: 57-66.

5 Manni L, Nikolova V, Vyagova D, Chaldakov GN, Aloe L. Reduced plasma levels of NGF and BDNF in patients with acute coronary syndromes. *Int J Cardiol*.2005;102: 169-171.

6 Sornelli F, Fiore M, Chaldakov GN, Aloe L. Adipose tissue-derived nerve growth factor and brain-derived neurotrophic factor: results from experimental stress and diabetes. *Gen Physiol Biophys* 28:179-83, 2009.

7 Chaldakov G. The metabotrophic NGF and BDNF: an emerging concept. *Arch Ital Biol* 2011;149: 257-263.

8 Chaldakov GN, Fiore M, Stankulov IS, Ghenev PI, Aloe L. Atherosclerotic lesions: possible interactive involvement of intima, adventitia and associated adipose tissue. *Int Med J* 2000; 7: 43-49.

9 Chaldakov GN, Fiore M, Hristova M, Stankulov IS, Triaca V, Ghenev PI, Aloe L. Adipose tissue-secreted molecules (adipokines): neuroimmune implications. *Clin Appl Immunol Invest* 2000; 1: 11-16.

2000: *CENACOLO MARCOFIORESCO* IN ROME

On a regular pattern, almost each Monday, Dr Marco Fiore invited me to a special diner (Italian, *cenacolo*) with his friends. *Cenacolo* derives from *Il Cenacolo Leonardesco*, the original title of Leonardo da Vinci's *The Last Supper*. In a traditional Italian way, it was an *ad libitum* (at one's pleasure) event, the table being full of food and wine, also grappa and Martini. Once in a summer, *cenacolo* was held on an open terrace near the moon and *Aqueducto Alexandrina*. Everything moved piano-piano, step-by-step, glass-by-glass, bottle-by-bottle, including a bottle of Martini dry, which was drunk by George 50. Later Marco told me that he and friends were a little bit surprised that I was very stable throughout the *cenacolo.*

"I will tell you the truth, *none* of you will betray me" (paraphrase from John 13:21) – this became the motto of *Cenacolo Marcofioresco*.

Grazie mille – said the moon and *Aqueducto Alexandrina*.

2002: NGF CONFERENCE IN MODENA

The 7th International Conference on NGF and Related Molecules was held on 15-19 May, 2002 in Modena, Italy. The conference was chaired by Laura Calza and Luigi Aloe. I attended the symposium as an invited observer - my Meeting Report was published in *Growth Factors* 2002; 20: 151-153. Leading NGF-ologits presented their SOS lectures, selected being published in 2004 issue of *Prog Brain Res* including our data as presented by Luigi [1]. Later, he invited me to collaborate in the preparation of this issue for publication. I waited my grandson birth that happened on 3 February 2003, spent with him a month in Varna and appeared at Leonardo da Vinci-Fiumicino International Airport of Rome in the beginning of March - welcomed by Luigi and Marco with a special *ciao* (meaning both hello and goodbye in Italy) from Leonardo da Vinci sculptured at the front entrance of the airport by a Bulgarian artist. I spent 3 months in Rome. It was a hard-and-pleasant work, sometimes overnight – then Luigi gave me the key of RLM's office that was 2-3 rooms next to my office, and I slept 3-4 hours in a couch until early morning before the arrival of ladies who cleaned the rooms in institute.

Back to the Modena-2002, I knew that Raina Kabaivanska, a Bulgarian *belcanto virtuoso* in Italian opera, is living in Modena. I also knew that she was born 6 years earlier than me in a house not far from my house in Burgas. And that our fathers knew each other. However, I had no courage to approach her house. Thus when backed home, I was unable to write "I met with HM RK" Instead, wrote *Un tributo per Raina* entitled "Ev-viva Riana Kabaivanska".

2003-2004: VISITING PROFESSOR IN KANAZAWA, JAPAN

Recommended by Professor Naofumi Mukaida, Head of Division of Bioregulation, University Cancer Research Institute in Kanazawa, I was awarded a fellowship from Japanese government for visiting professor, for 10 months since 1 June 2003. It was hard and pleasant work in a friendly atmosphere of Yoshinori Tomita, Boryana Popiv-

1 Chaldakov GN, Fiore M, Stankulov IS, Manni L, Hristova MG, Antonelli A, Ghenev PI, Aloe L. Neurotrophin presence in human coronary atherosclerosis and metabolic syndrome: a role for NGF and BDNF in cardiovascular disease? *Prog Brain Res* 2004;146: 279-289.

anova, Chifumi Fujii and Peirong Lu (now Professor of Ophthalmology in China). And my very "relaxants" Matsko and Kumiko, a grandmother and granddaughter, who welcomed me every day in a calm atmosphere of "Lilly", a coffee and lunch bar, near university, and the tall and noble man Sadao, the owner of restaurant "Noppo". In the lab, I tried to see whether mast cells might be a "master" in animal models of liver and lung cancer. Despite having not bad laboratory experience with these "master cells" (Steve Galli's term), the chance did not smile to me. Meanwhile, I found apoptotic images in lung metastasis specimens which fitted Mukaida's hypothesis [2].

Fortunately, I met excellent *tomodachi* (friends) in Kanazawa, Hiro Yamamoto and Shiichi Harada becoming my BHF. Together with Dr Mitsuru Kikuchi, Professor George Popov, Dr Anton Tonchev and my son, they helped me to easier be relieved from a depression I fallen in January-February 2004, again after its first attack in 1977-1979. Thus I was able to again enjoying pubs and bars and the cascade of transferring from one to another bar, Hiro's concept of "let us metastasize", a very benign phenomenon, especially in "Zadan".

2006-NOW: GUEST PROFESOR IN NIŠ, SERBIA

Couple of years before this honorable event I had many colleague-friends and a collaborative research with one of them, Professor Gorana Rančić at Department of Histology and Embryology, Medical Faculty in Niš, Serbia. In 2006 thanks to her nomination I was elected Guest Professor of Cell Biology at their Faculty. Consequently, I visited Niš frequently but never in the beginning of September. It may be such a chronological deficit that does not allow me to lecture in the "boulevard auditorium" of Leskovac, a city 45 km south of Niš. There, roštiljijada (in Serbian "roštil" means "grill", hence "Olympic grill") is held annually – a lot of meat, red wine and rakiya (plum or grape brandy, also popular in Bulgaria) are offered on the tables placed on the main boulevard at the beginning of September, the lectures lasting 5 days-and-nights. It may hopefully be happened to me in my next visit. Then, we may also visit the International IVF Clinic headed by another Serbian friend, Professor Miodrag Stioykovič.

2007: *DOCTOR HONORIS CAUSA* IN CLUJ-NAPOCA, ROMANIA

In 2005, an international student scientific conference was held in Novi Sad, Serbia. The youngsters have invited few oldsters. I was one of them and another was Professor Gheorghe Benga, Head of Biochemisty Department at University of Medicine and Pharmacy in Cluj-Napoca, Romania. He is a great name in the field of aquaporins (water channels), the discoverer of aquaporin 1. Instead, in 2003 the Nobel Committee acknowledged Peter Agre's contribution, not that of Gheorghe Benga, adding one more Romanian example to the Nobel Committee's ignorance list of discoverers like Nicolae Paulescu discriminated in favor of Frederick Banting and John Macleod in 1923 for the discovery of insulin.

Dr Benga nominated me for the honorary degree of *Doctor Honoris Causa*, The University Board elected me, and on 5 December 2007 a *Gala Extraordinara "Medicina, Arta,*

2 Tomita Y, Yang X, Ishida Y, Nemoto-Sasaki Y, Kondo T, Oda M, Watanabe G, Chaldakov GN, Fujii C, Mukaida N. Spontaneous regression of lung metastasis in the absence of tumor necrosis factor receptor p55. *Int J Cancer* 2004;112: 927-933.

Cultura" was held in the National Romanian Theater and Opera House. Thus, in the *matricula* of the 88-year-old University of Medicine and Pharmacy for the first time was enlisted the name of Bulgarian scientist, along with those of the Nobelists George Palade and Günter Blobel awarded in 2003. Later I visited *Terra Rumaneasca* several times to lecture and increase the number of BHF - Professor Dan Dimitraşcu, Dr Ion David, his charming wife Carmen and their son Flaviu, Dr Cristina Hotoleanu, *una donna molto bella*. And Professor Piero Portincasa from Aldo Moro University Medical School in Bari, Italy, who recently nominated me for Guest Professor in Bari.

2009 IN ROME: HER EXCELLENCY THE CENTENNIAL LIFE

Professor Rita Levi-Montalcini was born on 22 April 1909. In April 2009 many Italian institutions at governmental and scientific level honoured her centennial life. On 21 April 2009, Luigi Aloe organized a symposium on RLM-NGF couple, to commemorate her invaluable contribution to the understanding of the universe of neuronal life. Luigi told me that when invited RLM to present a lecture at the symposium, she replied: "I will lecture at the next symposium, Luigi".

Luigi also invited me, I accepted the gesture, arrived in Rome, gave Professor Rita Levi-Montalcini the Diploma of the Most Honored Member of the BGSCB, and presented a lecture on metabotrophic potentials of NGF and BDNF in cardiometabolic health and disease. In a way of *casa dolce casa* I proposed one more "ome sweet ome" designated "NGF-ome", that is, all the targets (cells, health, diseases, love) affected by NGF and related molecules. I also said that NGF deserves to be honoured "montalcinium" in the "Periodic table" of biomolecules, like, for example, einsteinium (Es) discovered in 1952, a year after NGF, and positioned No 99 between californium (Cf) and fermium (Fm) in Dimitri Mendeleev's Periodic table of chemical elements. Or, "God molecule", in analogy with Peter Higgs' "God particle", the boson.

After my talk, RLM said to me: "Giorgio, congratulations indeed!"

2010 IN VIENNA: BULGARIAN OF THE YEAR 2009

In the early 1800s, Ludwig van Beethoven took his dinner with glass of red wine, now bottled and named "9", because the Maestro composed 9th Symphony in his house in Heiligenstein, a village rich in vineyards and SPA (Latin, *Sanitas Per Aquam*), where Beethoven arrived to treat his deafness as advised by his doctors.

In the last months of 2009, *Wien Heute* (German, *Vienna Today*), a Bulgarian newspaper based in Austria, organized the nomination and voting for "Bulgarian of the Year 2009" in art, science, medicine, literatute, and sport.

In the middle of January 2010 I landed on Vienna international airport, moved to green CAT platfrom of the underground railway, welcomed by Saschka Zhurkova, the Editor of *Wien Heute*. Zhurkova, but in Austria she is officially known as Jurkov - such a deletion of "a" at the end, a masculinised version of family names became popular for Bulgarian ladies abroad. More important, before being Zhurkov, Saschka - together with her husband and two sons - courageously crossed the border between communism and democracy and luckily accommodated her family in Vienna.

Thus, at Vienna airport Mrs Zhurkov and two editorial board members welcomed me and together with the "green cat" reached the centrum of Vienna. Where *Cafe Central* also waited for us. Opened in 1876, *Central* became a place for many *stammgäste* (German, regulars, frequenters) belonging to intellectuals. With some exceptions – we also sat down there.

The ceremony of warding was held in Red House of "Mayer am Pfarrplatz" founded in 1683 in Grinzing, a peripheral area of Vienna, not far from Beethoven's house. The ceremony was under the patronage of Dr Antonia Parvanova, a member of the European Parliament, and our former student. She presented me with a diploma and medal for being elected Bulgarian of the Year 2009. I thanked her and *Wien Heute* reminding "to love each other", as written on 6 October 1802 by Beethoven in a letter to his brothers.

2012 IN YALTA: NATO ADVANCED RESEARCH WORKSHOP

Once on a summer time, thanks to the grant I was awarded from Grant Pierce (Univesity of Manitoba in Winnipeg, Canada) and Volodymir Mizin (State Medical University in Yalta, Ukraine) to present a lecture at NATO Advanced Research Workshop held 16-19 May 2012 in Yalta, Crimea, Ukraine. This was the second Big Event held in this hugged-by-mountain beautiful city, the first one being the meeting of Big Three (Churchill, Roosevelt and Stalin) held 4–11 February 1945 in Livadia Palace near Yalta. The only difference was that we discussed bioactive compounds countering the effects of radiological, chemical and biological agents, while Big Three focused on Europe's post-war reorganization (leaving Bulgaria under the Big Brother's communistic dictate).

During all 5 days in Yalta, the female black bear Winnie, brought from Winnipeg to Yalta by Grant Pierce, Alex Omelchenko and Elena and Pavel Dibrov, *sat and thought, sometime just sat* and listened the SOS lectures, including my talk on adipotoxicology and toxicrine activity of adipose tissue. Winnie also joined us during the rich LD, Grant and Alex ensured *ad libitum* honey for her. Finally, Geil (Grant's wife I named "The Spirit of Workshop"), Olivera Stanojlovic (from Belgrade, Serbia I named "Olympia in Science"), Christine (wife of the famous Dr Balwant Tuana I named him "The Commandment No 7"), Anna (a charmfulness from Armenia), Giorgi Kvesitadze (a big Georgian man who is 2 years younger than me), František Kolář (from golden Prague), Vladimir Jakovljevic (from Kragujevac, Serbia), Dragan Djiric (from Belgrade), Andrey Zagayko

(from Kharkiv, Ukraine), Boris Krylov (from St Petersburg, Russia), Yan Kyselovic (from Bratislava, Slovakia), the cardiac progenitor cells exposed to cerium oxide nanoparticles of Paolo Nardo from Rome, "it's not how much but where" in the cells of Donald Maurice and his charming wife from Kingstone, Canada, the polyphenol-rich wine concentrate "Enoant" of Yuriy Ogay from Yalta, the circulating angiogenic cells and their microRNAs of Micheal Kutryk (from Toronto, Canada), and, certainly, the philosopher Winnie broadcasted the signal of "SOS for *Homo sapiens*", to hopefully reach some politicians and businessmen, and make them altruistic to science and human health.

To *act, act, act*, a paraphrase of Winnie-the-Pooh's "think, think, think".

THE ESSENTIAL GEORGE: BHF, MD, PhD, DHC

Anyone who is to be happy, then, must have excellent friends.
Aristotle, from *Nicomachean Ethics*, 1170b19

Sine amicitia vita nulla est.
Marcus Tullius Cicero

During Christmas holidays-2010, I received a greeting card from Professor Marcia Hiriart from Mexico with a message: "May our growth factors continue to grow in a collaborative effort between our labs." Our evaluation revealed that this should be the thought of brain-and-heart friends (BHF) for the year 2010.

"Even longer" as Winni-the-Pooh answered to the question "We'll be friends forever, won't we, Pooh?"

In our lexicon, this is expressed as BHFF (brain-and-heart friends forever). Although, in his essay *On Friendship*, Michel de Montaigne discussed the mutability principle whereby friends can become enemies and *vice versa*. In ordinary life we must reconcile ourselves to the possibility that there are no friendships that we can rely on as bona fide permanent. But I do not like to believe that.

Forgetting *O my friends, there are no friends* (attributed to Aristotle) as well as *O my enemies, there is no enemy* (Nietzsche), I open Aristotle's *Nicomachean Ethics,* describing ethics and friendship. According to Aristotle the highest good for humans is *eudaimonia*, a Greek word for well-being or happiness. Aristotle argues that happiness is properly understood as an ongoing and stable dynamics, a way of being in action (*energeia*) specifically appropriate to the human soul (*psyche*) at its excellence (*arete*), its beauty (*kallos*), and the greatness of soul (*megalopsychia*). Book II Chapter 6 describes friendship (*philia*) is a virtue, an essential component of living well and appreciating each other's virtues. Aristotelian philosophy argues that one's friend is "another oneself". Much later, in May 1871, Arthur Rimbaud wrote a letter to his teacher commonly called the *Lettre du voyant* (Letter of the Seer), where expressed his famous maxim: *Je est un autre* (French, "I is another").

Brain-and-heart friendship provides a bridge between the virtues of intellect (brain) and those of feeling (heart/ soul). One should be responsive (outward, decoding signals derived from other people) and responsible (inward, following his/her inner compass), a *Homo interactomicus* (*H. reciprocans*), as illustrated in Albert Einstein's "If you have a apple and I have a apple, and we exchange the apples, each of us will have a apple only. However, if you have an idea and I have an idea, and we exchanged the ideas, you will have two ideas and I will have two ideas."

According to the network theory, the happiness tends to be correlated in social networks. When a person is happy, nearby friends have a 25 percent higher chance to also

be happy. Furthermore, people at the hub of a social network tend to become happier than those at the periphery. Something like hub proteins, which are able to form protein-protein interaction network. As well as a talk between Mind and Molecule where Mind got his Eureka moment: "He is a molecule precisely because he interacts with other molecules; he is nothing on his own" [1].

Although the evolution does not make moral distinction in the selection, and "one-eat-another" scenario [2] conjured up by the phrase "survival of the fittest" does bear much resemblance to everyday life, in the modern evolutionary biology, "survival of the nicest" is becoming appreciated – it up-regulates the cooperation as „natural" as competition, and altruism as natural as selfishness [3]. We need to find the right balance between the two - a story from A (alpha) to Ω (omega), that is, ΑΓΑΠΩ (*agapo*, Greek, love). As Ralf Emerson's *Man Thinkig* said "All things have two handles; beware of the wrong one."

"In the conditions of spiritual disintegration in which we live, modern man is "in search of a soul" [4]. As well as a BHF, where Apollonius and Dionysius get together, that is, Apollonysian life.

In the last as well as present century, science accelerates through a positive feedback effect, as predicted by the American historian Henry Adams. Thus, information begets more information, and knowledge begets more knowledge [5]. This acceleration, however, has a side effect: commercialization-driven wasteful competition including in biomedical research.

We should therefore ask ourselves where is Santiago Ramon y Cajal's devotion to "religion of the laboratory" we have lost in hard competition? Where is the friendly competition we have lost in commercialization? Reminding T.S. Eliot's questions:

Where is the wisdom we have lost in knowledge?

Where is the knowledge we have lost in information?

Emphatically, we need the replacement of commercialization with collaboration, selfishness with reciprocal helpfulness, *Survival of the Fittest* with *Survival of the Nicest*. The discovery of altruism growth factor (AGF) may facilitate this process.

Altogether, the filomics (Greek, *fillos* - friend) is superior than other "-omic" sciences, suggesting that, Human Phiolome Project should be launched tomorrow [6,7].

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1 Noble D. Prologue. Mind over molecules: activating biological demons. *Ann NY Acad Sci* 2008; 1123: xi-xix.

2 *The nature, red in tooth and claw* written in 1850 by the great English poet Alfred Tennyson in *Canto 56* of his poem *In Memoriam A.H.H. (*original title *The Way of the Soul*) dedicated to his fellow poet, Arthur Henry Hallam. This is before the publication of Charles Darwin's *On the Origin of Species* (1859) and Herbert Spencer's *The Principles of Biology* (1864) where he introduced the metaphor *Survival of the Fittest.*

3 Axelrod R, Hamilton W. The evolution of cooperation. *Science* 1981, 211, 1390-1396.

4 Roszak T. Science: a technocratic trap. In: T. Roszak*,* editor. *Where the Wasteland Ends.* Faber and Faber Ltd, London, UK.1972.

5 Will there be anything left to discover? A debate between John Horgan and Paul Hoffman. *Time Magazine USA* April 10, 2000.

John Horgan is the author of the book *The End of Science* (1997), Paul Hoffman is former editor of Discovery Magazine and past president of the Encyclopaedia Britannica. In this *Time* talk, John said: "Paul, you should jump on the end-of-science bandwagon before it gets too crowded."

In the last decade of 20th century other "end" books were also published: Francis Fukuyama's *The End of History* and David Lindley's *The End of Physics*.

Yet, someone will write *The End of Selfishness*.

6 Chaldakov G, Chaldakov N. *The Human: Thoughts, Feelings, Friendship*. Essays and Photographs. 2nd edition. Atelie'89 Varna. 2010 (in Bulgarian).

7 Chaldakov G. Philome: the genes of friendship. *LiterNet* 27 October 2010; 10 (131) (in Bulgarian).

1962-2012: THE JOY OF DOING SCIENCE AND EDUCATION IS A SUPREME KIND OF BRAIN-AND-HEART FRIENDSHIP

In his popular book *The Quark and the Jaguar: Adventures in the Simple and the Complex*, Murray Gell-Mann when explained what is the meaning of “to condense a message”, described a story with the elementary school teacher who assigned for home work to her class an essay consisted of 300 words [1]. One boy who spent the day playing around outdoors, scribbled the following on the next morning before going to school: "Yesterday the neighbours had a fire in their kitchen, so I leaned out of the window and yelled: fire, fire, fire…” In such a way, the story became of exactly 300 words.

Now, following this boy’s way of writing, I write “The brain is the most multiplex matter on the Earth. The brain is located in the head (Greek, *encephalon*). And in the heart, heart, heart…”

Chou-ju (Japanese, The longevity is a good thing)

Since I know René Descartes’ maxim *cogito ergo sum*, I wonder “How one can think without feel!” How can be “a thinking thing” without be a feeling thing. The brain-heart link is bidirectional – Antonio Damasio, Professor of Neurology in South California University in Los Angeles, replaced Descartes’ *cogito ergo sum* (the rationalism) with “We are not thinking machines, we are feeling machines that think” (the emotional rationalism). More can be found in Damasio’s books “In search for Spinosa: joy, sadness and feeling brain” and “The Mistake of Descartes: emotion, thought and the human brain”. Years ago Fridrich Nietzsche has been written: “There is more wisdom in your body than in your deepest philosophy”, in his book *Human, All Too Human*.

Since “a picture is worth a thousand words”, a collage called *Friendorama* made by Dr Vesselka Nikolova, a BHF and renowned cardiologist in Varna and in Göttingen, Germany, and Kiril Todorov, an expert in computer design, is shown on the front cover of the book.

My first cordial wish to all the BHF is to enjoy a creative longevity illustrated above calligraphically by Professor Hiroshi Yamamoto, Dean of the Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Kanazawa, Japan.

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1 Murray Gell-Mann. Let’s call it plectics. *Complexity* 1995/96; 1 (5).
Murray Gell-Mann. Plectics: The study of simplicity and complexity. Talk delivered to the symposium "Frontiers of Science" held in Coimbra, Portugal, 1999.

Murray Gell-Mann is Professor of Physics at Institute of plectics in Santa Fe, California. He is the discoverer of “strange and charming particles” he named quarke. These brought to him 1969 Nobel prize in physics.

In these articles, Gell-Mann explains the origin of "plectics” – in Greek *plektos* means “braided”. The word "complex" comes from *plexus*, originally meaning braided, and *com*, meaning together, hence braided together. "Simple" comes in a similar way from roots meaning once folded. Hence "plectics" covers both simplicity and complexity.

The fact is the sweetest dream that labour knows. www.chaldakov.com
My long scythe whispered and left the hay to make.
Robert Frost, *Mowing*

www.chaldakov.com
Photograph by Nick G. Chaldakov

My second cordial wish to all the BHF is to obtain “facts” in support of their hypothesis illustrated above by a poem and photograph.

LETTERS FROM FRIENDS

Dear George,

Than you very much for the useful book “Pharmacotherapy of Obesity” you sent me. Thank you for your significant real and virtual presence in our scientific and daily life. Be happy and healthy.

With best wishes,
Sincerely yours,
Iskren Kotzev

Sunday, February 22, 2009 12:55:39 PM

Professor Iskren Kotzev is Head of Department of Gastroenterology, St Marina University Hospital, Varna, Bulgaria.

Caro nuovo amico mio George,

It was really a pleasure meeting you last Sunday. Tommaso and I really enjoyed the conversation with you and you are the most welcoming person I ever met in my life! I am sorry we did not have the chance to say good bye, but we came to Palestrina with other friends, not with our own car, so we had to respect their timing and could not wait for you to come back from you walk.

Thank you very much for the invitation at the symposium, I will try my best to find a travel grant. As I mentioned alreday, I am attending the meeting of the society for neuroscience which will be held in Chicago from October 17 to October 21, so it might be a little difficult to fit dates and expenses. I would love to keep in contact with you not only for your very nice sympathy but also to share scientific interests and maybe future projects. Thank you for sending me your papers, I am preparing a paper on the endogenopus lipid I am studing and the involvement of hypothalamic oxytocinergic tone in mediating its prosatiety effects. I will send you the draft as soon as it is done and I would be honored to have both your and Dr Aloe's comments.

Un abbraccio,
Silvana e Tommaso

Tuesday, April 28, 2009 1:54 PM

Dr Silvia Gaetani, Department of Pharmacology, Sapienza University, Rome, Italy

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Dear George,

I learned that the life is a passage, transition of a great importance. So that I do my best to spend it with friends we sharing a common philosophy and aims. You are one of them. What remains is to have *zelju za zivotom* (Serbian, desire for life) as my father used to say when he was 102-year-old.

Cordially yours,
Tomislav

Saturday, October 3, 2009 4:38:50 PM

Dr Tomislav Djokic is Professor of Physiology (and Art) in Belgrade, Serbia.

Caro George,

Personally, particular aspects that impressed me the first times I met you in 1995, was not only your scientific knowledge and relationship with your students, but also your personal and human qualities outside the scientific community, friends and relatives. I remember when I met your mother the first time in Burgas and the last time in your home in Varna when she was in bed with hemiparesis with great difficult to speak and your patient to teach her how to pronounce my name before my forthcoming visit in Varna. Your dedication and your affection for your mother. I should have much more to say about your day-by-day life, about care and dedication to Antoanetta, Nikifor and Nikolai.

George, science and human qualities (*Science e Coscienza*) are not common to human being, but to great man. Indeed, I can tell that to my family and relatives, as well as to my close friends I always told more the latter qualities than the former ones.

George a man for all season of life.

All the best and *lunga vita all'amico* George!

Luigi Aloe
AD MMXII, Rome

Institute of Cellular Biology and Neurobiology, National Research Council (CNR), Rome, Italy

CURRICULUM VITAE

George Nikov Chaldakov, MD, PhD

23 February, 1940, Burgas, Bulgaria
Married: one wife, one son, one grandson

Laboratory of Cell Biology
Medical University
BG-9002 Varna
Bulgaria
E-mail: chaldakov@yahoo.com

Editor-in-Chief

(i) *Biomedical Reviews*, An International Journal of Cell Biology of Disease
(ii) *Adipobiology*, An International Journal of Adipose Tissue in Health and Disease

Chairman

(i) Bulgarian Society for Cell Biology
(ii) International Symposium on Adipobiology and Adipopharmacology (ISAA)
(iii) Biomedical Forum, a CME Program

Guest Professor

(i) University Medical School, Kanazawa, Japan (2003-2004)
(ii) University Medical School, Nis, Serbia (2006-)
(iii) Aldo Moro University Medical School, Bari, Italy (2012-)

Doctor Honoris Causa

(i) University of Medicine and Pharmacy, Cluj-Napoca, Romania (2007-)

Recent field of research

Cardiovascular adipobiology, Translational cardiometabolic research

Teaching medical students

Cell biology, Neurobiology

Supervisor of PhD Thesis on: human atherosclerosis, focusing on adventitial remodeling; rat spermatogenesis; rabbit ciliary body of the eye; NGF and BDNF in patients with metabolic syndrome.

Membership

International Atherosclerosis Society, European Atherosclerosis Society, International Academy of Cardiovascular Sciences, European Vascular Biology Society, Canadian Obesity Network.

CONTRIBUTIONS

Ask yourself for each of your thoughts: is it a new one?
Carl Gustav Jung

I. Concept of secretory function of vascular smooth muscle cells

1. Chaldakov GN, Nikolov SD. Ultrastructure of the arterial smooth muscle cell. In: Wolf S, Werthessen NT, editors. *The Smooth Muscle of the Artery*. New York City: Plenum Press. *Adv Exp Med Biol* 1975; 57:14–20.

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4. Chaldakov GN, Vankov VN. Morphological aspects of secretion in the arterial smooth muscle cell, with special reference to the Golgi complex and microtubular cytoskeleton. *Atherosclerosis* 1986; 61: 175-192.

II. Hypothesis of tubulin-targeted pharmacology for atherosclerosis

5. Chaldakov GN. Antitubulins – a new therapeutic approach for atherosclerosis? *Atherocslerosis* 1982; 44: 385-390.

6. Chaldakov GN, Vankov VN. Antifibrotic approach in the therapy of arterial occlusive diseases: new considerations. In: G. Trubestein, editor. *Conservative Therapy of Arterial Occlusive Disease*. Stuttgart, New York, Georg Thieme Verlag, 1986, p. 224-226.

III. Concept of (cardiovascular) adipobiology

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14. Chaldakov GN, Guest Editor. *Adipobiology of Disease*. *Immun Endocr Metab Agents Med Chem* 2007; 7: 105-173.

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From adipose tissue protein secretion to adipopharmacology of disease. *Immun Endoc Metab Agents Med Chem* 2007; 7: 149-155.

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19. Chaldakov GN, Neşe Tuncel N, Beltowski J, Fiore M, Rańćić G, Tonchev A, Panayotov P, Evtimov N, Hinev A, Anakievski D, Ghenev P, Aloe L. Adipoparacrinology: an emerging field in biomedical research. *Balkan Med J* 2012; 29: 2-9

IV. Concept of neuroadipology

20. Chaldakov GN, Fiore M, Tonchev AB, Hristova MG, Rańĉiĉ G, Aloe L. The adipose tissue as a third brain. *Obesity Metab* 2009; 5: 94-96.

21. Chaldakov GN, Fiore M, Tonchev AB, Hristova MG, Nikolova V, Aloe L. Tissue with high intelligence quotient: adipose-derived stem cells in neural regeneration. *Neural Regen Res* 2009; 4: 1116-1120

22. Sornelli F, Fiore M, Chaldakov GN, Aloe L. Adipose tissue-derived nerve growth factor and brain-derived neurotrophic factor: results from experimental stress and diabetes. *Gen Physiol Biophys* 2009;28:179-183.

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V. Concept of metabotrophic potential of neurotrophins

24. Chaldakov GN, Fiore M, Hristova MG, Aloe L. Metabotrophic potential of neurotrophins: implication in obesity and related diseases? *Med Sci Monit* 2003;9:HY19-21.

25. Chaldakov GN, Fiore M, Stankulov IS, Manni L, Hristova MG, Antonelli A, Ghenev PI, Aloe L. Neurotrophin presence in human coronary atherosclerosis and metabolic syndrome: a role for NGF and BDNF in cardiovascular disease? *Prog Brain Res* 2004; 146: 279-289.

26. Chaldakov GN, Fiore M, Tonchev AB, Aloe L. Adipopharmacology, a novel drug discovery approach: a metabotrophic perspective. *Lett Drug Design Discov* 2006; 3: 503–505.

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28. Chaldakov GN, Tonchev AB, Aloe L. NGF and BDNF: from nerves to adipose tissue, from neurokines to metabokines. *Riv Psichiatr* 2009;44:79-87.

29. Chaldakov G. The metabotrophic NGF and BDNF: an emerging concept. *Arch Ital Biol* 2011;149:257-263..

Selected list of supported participations

Invited Speaker, International Symposium on Smooth Muscle of the Artery, Heidelberg, West Germany (1973)

Invited speaker, International Symposium of Arteriosclerosis, Münster, West Germany (1977)

Invited speaker, International Symposium of Atherosclerosis, West Berlin, Germany (1982)

Invited Speaker, World Congress of Angiology, Rochester, Minnesota, USA (1983)

Invited lecturer, Department of Anatomy, University of Illinois Medical School, Chicago, IL, USA (1983)

Invited speaker, European Vascular Biology Symposium, Nyon, Switzerland (1984)

Invited speaker, European Cytoskeletal Society Symposium, Bilefeld, West Germany (1985)

Invited lecturer and consultant, Department of Biology, Odense University, Odense, Denmark (1995)

Invited speaker, Osmangazi University Medical School, Eskisehir, Turkey (1996)

Invited speaker, Meeting of the International Neuropeptide Society, Antalya, Turkey (2001)

Invited lecturer, *Charite* Medical School, Humboltd University, Berlin, Germany (2001)

Invited observer, The 7th International Conference on NGF and Related Molecules, 15-19 May, 2002, Modena, Italy

Invited speaker, Physiology Congress, Edirne, Turkey (2010)

Invited lecturer, Medical and Pharmacy Faculty, Near East University, Nicosia, North Cyprus (2011)

Invited speaker, NATO Advanced Research Workshop on Bioactive Compounds Countering the Effects of Radiological, Chemical and Biological agents, 16-19 May 2012, Yalta, Crimea, Ukraine.

SELECTED LIST OF PEER-REVIEWED PUBLICATIONS

1. Chaldakov GN, Kokosharov PK. An intracristal structure in rat liver dumbbell-shaped mitochondria. *Acta Morphol Acad Sci Hung* 1973; 21: 149-154.

2. Chaldakov GN, Nikolov S. Ultrastructure of modified smooth muscle cell. In: Wolf S, Werthessen NT, editors. *The Smooth Muscle of the Artery*. New York City: Plenum Press. *Adv Exp Med Biol* 1975; 57:14–20.

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12. Chaldakov GN, Ghenev PI. Intermediate filaments in arterial smooth muscle cells: structure, origin, and development. *Folia Morphol* 1981; 29: 364-366.

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15. Nikolov S, Chaldakov GN, Gabrovska M. Tubular pattern of filaments of elastic fibers. *Anat Anz* 1984; 165: 57-64.

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17. Chaldakov GN. The ciliated smooth muscle and endothelial cells. *Atherosclerosis* 1985; 56: 251-256.

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ry-state smooth muscle cells from the rabbit artery wall. *Exp Pathol* 1987; 31:1-9.

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25. Chaldakov GN, Nara Y, Horie R, Yamori Y. A simple and reliable method for visualization of arterial autonomic nerve plexus by scanning electron microscopy. *Acta Morphol Neerl Scand* 1987; 25: 273-277.

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