The serendipity of Homero Augusto Campos Iturrizaga

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y en memoria del Dr. Augusto Campos
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Popularized in Physiology by Cannon (Merton and Barber, 2004), the little-used term *Serendipity* lends itself to start talking about someone we want to remember. Both of its meanings, *serenity* and *the faculty of finding valuable things not sought for*, correspond to Dr. Campos. This was what Dr. Guillermo Whittembury mentioned that day of 2005, during the speech on the naming ceremony after Dr. Campos of the Auditorium of the School of Medicine José María Vargas of Venezuelan Central University (Wittembury, 2005). It was an act driven, above all, by Dr. Manuel Velasco's proposal, together with the other members of the Pharmacology Chair, that same Chair that Dr. Campos helped consolidate since his incorporation in 1969, attending the invitation from our also beloved and always remembered Dr. Edmundo Vallecalle (Álvarez, 2005), to contribute to the development of a Department of Physiological Sciences which members would assume full-time research and teaching as their goal in life.

And, said Dr. Whittembury, it was his *serendipity* what once got him out from what he initially believed had been a catastrophe. After having applied some doses of cocaine to the dogs of the experiments of his Master, Dr. Carlos Gutierrez-Noriega, for a study on cocaine addiction, one of the dogs presented a catatonia reaction. He thought that the animal was dying and, in an act of compassion, he injected a barbiturate to help the dog to die peacefully. Surprisingly, the catatonia reversed and the dog got up and ran away! Dr. Gutierrez incorporated him as an assistant to the Institute of Pharmacology in Lima. It was 1948 and he was just at the beginning of his studies in Medicine. This casual discovery made his teacher follow an exciting line

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of research that was later frustrated by a fatal accident suffered by Dr. Gutierrez in 1950.

It is not the purpose of this article to make a biography of Dr. Campos because there are many reviews in this regard (Fuenmayor, 2012). The aim is rather to satisfy the proposal of his disciples, and some of my colleagues, who had the joy of having him as an undergraduate faculty and later as the Tutor of our postgraduate studies. The proposal was to make a succinct narrative of his main and last line of research in which we had the pleasure and honor to accompany him: **The reflex that modulates by inhibition the peripheral sympathetic activity and blood pressure.**

Dr. Campos began as a researcher in 1948 at San Marcos de Lima University. He then complemented and nurtured his foundations as a researcher for 5 years between the universities of Wisconsin and Minnesota in the United States, when he obtained sufficient experience, knowledge, and maturity to make the leap from Classical Pharmacology to Neurotransmitters Pharmacology. Since his beginnings at the Vargas Medicine School, Pharmacology Chair, he systematized and focuses his line of research on the role that histamine could play as a neurotransmitter when it acts on H_3-type receptors. H_3-type receptors were known and described at the level of the central nervous system, but they were little-noted regarding their possible role in the control of the peripheral autonomic nervous system.

Dr. Campos undergraduate classes were authentic experiences on the autonomic nervous system. His answer to our question of why he had not stayed in the United States was for us of significant reflection, still in force:

> "*As a researcher, I need to follow the opinion of my motivation, and it is difficult for me to subject my activity to a pre-established routine. This conception needs to get away from the pressure to publish a certain number of papers in certain lapses, the pressure that is exerted on the researchers by some academic institutions in these developed countries, at the expense of the motivation.*"

After 14 years of intense and systematic work, he presented his paper entitled *Histamine and the sympathetic system of the rat vas deferens* at the First Inter-American Congress of Pharmacology and Therapeutics (Campos, 1983), thus beginning his line of research which steps I present here below.

1. He discovered that the chronic unilateral sympathectomy of rat vas deferens causes a bilateral decrease in histamine levels, suggesting the presence of a nerve pathway containing histamine (Campos, 1988).

2. Together with Briceño, he surgically sectioned different levels of the rat vas deferens and measured histamine in each one of them to demonstrate and define the distribution of histamine-containing pathway adjacent to the sympathetic system (Campos and Briceño, 1992).

3. Magalgi, Israel, and himself confirmed that the activity of L-histidine-decarboxylase, an enzyme responsible for catalyzing the decarboxylation of

histidine to form histamine, decreases in parallel to the histamine content in the above model, when the same surgical sections are made (Magaldi *et al.*, 1993). This demonstration happened after he proposed, together with Dominguez and Sosa, that alpha-fluoromethylhistidine, an inhibitor of L-histidine-decarboxylase, induces arterial hypertension (Domínguez *et al.*, 1991).

4. By using L-histidine-decarboxylase as an activity marker, and by stimulating the sympathetic pathway of the rat vas deferens, he demonstrated the existence of a neuron that contains histamine in the periphery. Simultaneously, he proposed together with Magaldi, Israel, and Acuña a new model of arterial hypertension induced by the inhibition of histamine biosynthesis with alpha-fluoro-methylhistidine (Campos *et al.*, 1996; Acuña *et al.*, 1998).

5. He demonstrated that the stimulation of a histamine-containing neuron is dependent on the functional integrity of the noradrenergic neuron (Campos and Domínguez, 1995).

All this work allowed him to propose a model of neuronal regulation mechanism in which there is **a reciprocal contralateral inhibitory modulation of the peripheral sympathetic nervous system**, hitherto not taken into account, could be represented. Such a mechanism could contribute to elucidating what we continue to call "essential" arterial hypertension.

With this conclusion, he motivated us to accompany him in the next two stages of his research: the clinical verification of his experimental findings, and the demonstration of the histological-structural position of this reflex.

We began to see him fully introduced to us in hospital sets. Together with Romero, Montenegro, Velasco, Alvarez, Urbina, Alvarado, Navas, and perhaps some other names of our fellow clinical researchers and collaborators who I apologize if I do not name them, we began to structure a Clinical Laboratory where we would tests this hypothesis, such as the "Tilt-test", the "Treadmill", the use of edrophonium, and the "hand grip". It did not take long for that laboratory to produce the first clinical verification of his experimental research (Campos *et al.*, 1999; Alvarado *et al.*, 2008). The experience with our research in critically ill patients with pathologies that induce states of autonomic hyperactivity ("*Histamine regulates norepinephrine release in the peripheral nervous system in humans. Clinical verification in two pathologies that present autonomic hyperactivity: tetanus and Guillain Barre syndrome*", submitted for consideration for publication) and our first findings of correlation of blood histamine and norepinephrine levels in those patients who had criteria for essential arterial hypertension were also exciting and gratifying.

There was no truce. To arrive at the laboratory was to meet that permanently thinking being, affected by acute *serendipity* that seemed to be over-stimulated by those events of clinical correlation. His deductive power and permanent critical spirit, stimulated by the endless bibliographical research and discussion sessions in the different congresses, had led him to the need to demonstrate the existence of a peptidergic pathway as an integral part

of the modulating reflex (Campos *et al.*, 1998). Flor, my wife, classmate, and also his student, was just getting off the plane after completing her neuroscience doctorate when she receives his suggestion: "To structurally demonstrate the proposed peptidergic pathway mediated by substance P".

But we are in the ship of life, with its many avatars. Devoting to scientific research by then looked uphill, the situation in our country had become increasingly adverse and we were forced to change course. In our absence we got the news: the "*namesake*" (that's how he used to tell me) said goodbye.

I only allow myself to remember him with joy, and I keep a cartoon that he once brought from Brazil and which, laughing, he placed on the door of the laboratory:

"Teoria é quando tudo é conhecido e nada funciona.
A prática é quando tudo funciona e você não sabe o porquê.
Neste laboratório, combinamos teoria e prática: nada funciona...
e não se sabe por que"

"*Theory is when everything is known, but nothing works.*
The practice is when everything works, but you don't know why.
In this lab, we combine theory and practice: nothing works...
and you don't know why "

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