

Ion channels, transporters and cancer (“INCA2015”): an international meeting in honor of Prof. Dr. Walter Stühmer

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Ion channels and transporters (ICTs) are well known historically to be expressed in so-called ‘excitable’ cells, such as neurones, muscles, and neuroendocrine cells. Then, a range of classically ‘non-excitable’ cells (such as fibroblasts, epithelial, endothelial cells, and glial cells) were also found to express functional ICTs including voltage-gated ion channels. Although much work was done on ICTs expressed in various cancer cells, due to the relative ease with such cells can be cultured, it was not until the 1990s that scientists started questioning formally what ICTs were doing in cancer cells and whether such ionic activity contributed to the cancer process, including its many different facets and stages. Thus, a new field was born! While ion channel biophysicists were quick to embrace this new field, it took much longer for cancer scientists and oncologists to be convinced. An obvious early criticism was that it would not be possible to distinguish ICTs in cancer cells and tissues from those expressed widely elsewhere in the body, especially in a therapeutic context. However, we now know that ICTs can be specific to cancer qualitatively and/or quantitatively, for example, by being particular splice variants, by having expression levels significantly different to normal, and by occurring in specialized macromolecular complexes. Ultimately, the increasing weight of the experimental evidence

meant that clinical scientists are also being converted! Over this period, four international meetings were held to discuss progress. The first meeting was organized by Walter Stühmer and us in November 2007 and took place at Ringberg Castle, the special venue of the Max-Planck Society. This was followed in March 2010 by a meeting in Florence organized by Annarosa Arcangeli. The third meeting took place in Würzburg in September 2012 and was organized by Albrecht Schwab. Two reports of these meetings were published (Fraser and Pardo 2008; Pedersen and Stock 2013) and a Theme Issue of the Philosophical Transactions of the Royal Society followed (Djamgoz et al. 2014). By the time of the fourth meeting (“INCA2015”—<http://www.inca2015.com/>) at Imperial College London in September 2015, organized by Mustafa Djamgoz in association with the CRUK Centre and the Cancer Engineering Network of the College, the field had consolidated substantially, and it had become clear that ICTs are in all cancers (primary and/or secondary). The meeting covered these and several different cancers including those most difficult to treat, such as pancreatic cancer. Important highlights were the emerging *in vivo* evidence, systems pathophysiology, even natural products with anti-cancer properties targeting ion channels.

The INCA2015 meeting was held in honor of Walter Stühmer, who has been a pioneer and champion of the field of ‘ICTs and cancer’. In fact, his contributions to cell physiology and pathophysiology are much wider than this, and almost every one of his 200 or so papers represents a milestone in the field. His achievements are not only the result of inspiration and hard work but also of a life-long commitment to research driven by curiosity with a philanthropic attitude.

Born in Bogota (Colombia) as the son of a German–Italian couple, Walter spent his early years in close contact with the kind biological richness and diversity that would

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be only a dream for most European naturalists. Very soon he developed a fascination for nature, later combined with a keen interest in electronics. He built all sorts of devices during his early adolescence in Spain, which probably drove his decision to study physics in Germany. After earning a diploma in nuclear physics, he discovered the possibility of combining his scientific passions and decided to pursue a PhD in biophysics. That took him to the laboratory of Franco Conti in Camogli, Italy, where work was centered on a rather physical view of ion channels, such as the effects of hydrostatic pressure. After his PhD, he worked for some years with Wolf Almers in Seattle, mainly on ion channels of skeletal muscle. During this period, he ‘upped’ the technology, introducing improvements in the design of several electrophysiological instruments, and also designed some in full. Basically, each time he needed to answer a new scientific question where proper measurement was a problem, he simply designed a new device that could do the job. This included the ‘loose patch clamp’, which enabled the lateral motility of ion channels on muscle membranes to be followed.

He returned to Germany (Göttingen) in 1983 and has been associated with the Max-Planck Society ever since, first at the Max-Planck-Institute for Biophysical Chemistry (in Erwin Neher’s department), and then as a scientific member of the society and director at the MPI of Experimental Medicine, only 2 miles down the hill. His experiments enabled measurements that would seem impossible for most of us even today, such as the kinetics of ion channels at the inner mitochondrial membrane and the noise fluctuations in gating currents. He also started exploring the possibility of understanding the intimate mechanisms of function in ion channels by a combination of molecular biology (emerging at the time) and biophysics. He was the scientist who deciphered the structural features responsible for essentially all relevant properties of sodium channels. Voltage dependence, selectivity, or inactivation were all explained by his work. He (and others) later extended this approach to the understanding of other channel families (adenosine receptors and cyclic nucleotide-gated channels, among others), the characterization of a number of natural compounds affecting ion channels. His technical contributions also continued, such as applications of total internal reflection microscopy and complex optogenetic approaches. He received several awards, including the A.

V. Humboldt/J.C. Mutis Prize, the Cole Award of the Biophysical Society, Herlitza Prize (Torino), and the Cátedra Ramón y Cajal (Mexico).

During the last 20 years, a major part of Walter’s effort has been devoted to the field of ICTs and cancer, searching for both the understanding of the mechanisms by which ICTs are so relevant to oncology, and foremost, for ways of applying this knowledge to design better treatments for patients. The latter—people—is what really always matters to him. Throughout his career, he has maintained that good science can only be done in an atmosphere of healthy personal relations, where competitiveness is only a result of passion for science, and not an aim in itself, where the scientist is first a person always deserving consideration and whose creativity should always be promoted. Walter has always endeavored to be involved in initiatives to make it possible for scientists working in places where the conditions are not favorable to do research. He has tried consistently to make it possible for talent and creativity not to be hindered by geographical or financial conditions. He has participated in many courses in developing countries, has given all sorts of support to scientists coming from less-favored regions, and has promoted young scientists with projects such as the European Neuroscience Institute network (with E. Neher and D. Richter). Among other editorial activities, Walter has been a very conscientious and supportive Editor of the European Biophysics Journal for over 20 years, being the journal’s expert in ion channels and thereby attracting papers in this area.

This Special Issue comprises papers that were presented at the INCA2015 meeting but not restricted to it. Many of the contributors are friends or colleagues of Walter. If not, they will certainly have been influenced by his research at some point in their careers. We hope that the issue will help keep up the momentum in the field and encourage new investigators to enter it. Cancer now is one of the biggest killers of man, with one out of two and three men and women, respectively, currently expected to be diagnosed with some form of cancer during his/her lifetime. Although great advances are being made in the clinical management of cancer all the time, there is still significant unmet need as regards early, definitive, functional diagnoses, and long-lasting, non-toxic effective therapies. In these regards, there would seem no doubt now that ICTs offer much potential as novel cancer targets.

INCA 2015 participants



Walter, equipped for his second passion besides science:
flying gyrocopter (photo courtesy of A. Sánchez)

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