

Cover page: The Synthetic Lethal Rosette

Aberrant mitotic phenotype found in BRCA1-deficient cells treated with the PLK1 inhibitor Volasertib. Cells become giant and multinucleated and acquire a flower shape, with nuclei arranging in a circular disposition around a cluster of centrosomes. Blue (DAPI: nuclei), Green (FITC-phalloidin: actin cytoskeleton), Red (γ -Tubulin: centrosomes).

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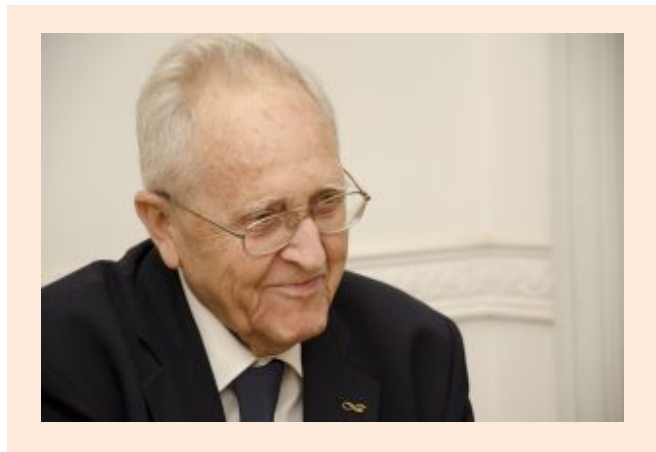
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IN MEMORIAM
HORACIO G. PONTIS
(1928–2019)



Horacio Guillermo Pontis, born in Mendoza (1928), graduated in chemistry and obtained the Ph.D. (1953; Dir.: V. Deulofeu) from the University of Buenos Aires. After working for three years with Dr Luis F. Leloir—where he approached to carbohydrate metabolism—he stayed successively at King College (UK), Durham University (UK) and finally at Karolinska Institutet and University of Stockholm—where his attention turned to enzymology studies. After returning to Leloir’s lab (1960), he embarked on plant biochemistry studies. In his search for clues about fructans, Dr. Pontis’ lab synthesized not only UDP-fructose but also fructose-2-phosphate, which two decades later cleared the way for the chemical synthesis of fructose-2,6-bisphosphate (a key glycolysis modulator).

From 1968 to 1977, he was the director of Dept. of Biology – Fundación Bariloche. In Nov. 1971, Bariloche hosted the SAIB Annual Meeting, being elected Dr. Pontis the President of SAIB (1972).

This reunion was followed by the Symposium “*Biochemistry of the glycosidic linkage*” with the presence of four Nobel Prizes (C. Cori

(1947), G. Cori (1947), F. Lynen (1964), L. F. Leloir (1970)). However, his “*mi mejor experimento y experiencia de formación*” came to a halt-in when the Bariloche lab was closed (1977).

In 1979, Dr. Pontis moved to Mar del Plata where over time his outstanding capacity for innovation launched Instituto de Investigaciones Biológicas (IIB) – U. N. Mar del Plata, Fundación de Investigaciones Científicas (FIBA) and Centro de Investigaciones Biológicas (CIB).

In any site, Dr. Pontis maintained active research groups that trained graduate and post-graduate students generating a steady flow of important contributions to plant biochemistry. The research international community acknowledged these accomplishments, such as American Society of Plant Biologists that named him Correspondent Member. In his scientific activities, Dr. Pontis has been member of the National Research Council of Argentina (1961; CONICET), and Biochemistry Professor –at the UBA and at Universidad Nacional de Mar del Plata. The former and the later institutions recognized his academic performance designating him Emeritus Investigator and Emeritus Professor, respectively.

Dr. Pontis’ story rose from limited beginnings—in Deulofeu’s and Leloir’s labs—to international scientific prestige. In this context, the challenge to overcome adversity during shameful periods in Argentine history honors not only his willingness but also his enthusiasm.

Ricardo Wolosiuk

Schedule	Tuesday November 5		Wednesday November 6	Thursday November 7	Friday November 8
8:30-9:00	WORKSHOPS Workshop Accreditation				
9:00-11:00	Biochemistry Education Workshop	1 st Workshop On Drug Discovery	Oral Communications Room Jacaranda PL-Co1, PL-Co2, PL-Co4 to PL-Co6, PL-Co9, PL-C12, ST-02, BT-Co2 Room Los Ceibos CB-Co1 to CB-Co4, CB-Co7 to CB-C10, ST-Co1	Conferences Room Lapacho <i>Robert Gennis</i> <i>Francisco Barrantes</i>	Oral Communications Room Jacaranda PL-Co3, PL-Co7, PL-Co8, PL-C10, PL-C11, PL-C13, PL-C14, PL-C15 Room Los Ceibos MI-Co1 a MI-Co6, BT-Co1, CB-Co6 Room Lapacho LI-Co1 to LI-Co5, ST-Co3, CB-C11, CB-Co5
11:00-11:30			COFFEE-BREAK		
11:30-12:30			Plenary lecture <i>Bruno Amati</i> Room Lapacho	IUBMB Jubilee Lecture <i>Philip D. Stahl</i> Room Lapacho	“Hector Torres” Plenary Lecture <i>Alejandro Colman Lerner</i> Room Lapacho
12:30-14:30			LUNCH TIME		
14:30-16:30			Symposia <i>Lipids</i> Room Jacaranda <i>Plants</i> Room Los Ceibos <i>Signal Transduction</i> Room Lapacho	Symposia <i>Cell Biology</i> Room Jacaranda <i>RNA</i> Room Los Ceibos	Symposia <i>Microbiology</i> Room Los Ceibos <i>PABMB</i> <i>Young Investigators</i> Room Jacaramda
16:30-17:00			COFFEE -BREAK		
16:30-18:30			POSTERS BT-Po1 to BT-Po6 CB-Po1 to CB-P15 MI-Po1 to MI-P18 PL-Po1 to PL-P15 ST-Po1 to ST-P13	POSTERS BT-Po7 to BT-P12 CB-P16 to CB-P31 EN-Po1 to EN-P11 MI-P19 to MI-P37 PL-P16 to PL-P32	POSTERS BT-P13 to BT-P19 CB-P32 to CB-P47 LI-Po1 to LI-P15 MI-P38 to MI-P49 PL-P33 to PL-P48
			Opening Ceremony Room Lapacho		
			<i>In memoriam of</i> Horacio Pontis Room Lapacho		
18:30-19:30			EMBO Keynote Lecture <i>F. Gisou van der Goot</i> Room Lapacho	“Ranwel Caputto” Plenary Lecture <i>Maria Elena Alvarez</i> Room Lapacho	Closing Ceremony Room Lapacho
			Cocktail 20:00 hs	SAIB Assembly 19:45 hs	Dinner 20:00 hs

EN-P07

A CHEMICAL BIOLOGY APPROACH TO UNDERSTAND THE REGULATION OF FULL-LENGTH PHOSPHOINOSITIDE-DEPENDENT PROTEIN KINASE 1 (PKB)

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Phosphoinositide-dependent protein kinase 1 (PDK1) is a master AGC kinase that phosphorylates at least other 23 AGC kinases, being PKB/Akt the most relevant substrate downstream of PI3-kinase, important for growth and cell survival, and a drug target for cancer treatment. Over the years, our laboratory studied and characterized in detail the catalytic domain of PDK1, as well as the selective activation of substrates such as SGK or S6K, which in order to be phosphorylated require a docking interaction with a hydrophobic site in PDK1 termed the *PIF-Pocket*. However, this is not the case of Akt/PKB, since it can be activated in a *PIF-Pocket* independent way. On the other hand, up to date little is known about the mechanistic and structural details of PDK1 full length. Therefore, we are using an interdisciplinary approach to understand how the full-length protein is regulated and how this regulation mechanism can be manipulated to specifically inhibit the activation of PKB/Akt. As a result of a medium-scale screening of small compounds we carried out using AlphaScreen technology, we validated a series of small compounds "hits" that modulate PDK1 structure by interaction at different sites on PDK1. We performed hydrogen/deuterium exchange (HDX) experiments and crystallization screenings to understand the structure of full-length PDK1 and how it can be modulated with small compounds. We here present a series of results obtained using HDX on full-length PDK1 and the crystal structure of the catalytic domain of PDK1 bound to a small compound identified in our screening. We also present our *in vitro* studies to understand the oligomerization of PDK1 visualizing single particles by using STORM fluorescence microscopy. Finally, we integrate our data to present an updated model on the molecular mechanism of regulation of PDK1.

EN-P08

KINETIC AND STRUCTURAL CHARACTERIZATION OF GALACTINOL SYNTHASE FROM *BRACHYPODIUM DISTACHYON*

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Raffinose (Raf) is an α -1,6-galactosyl extension of sucrose that is used for carbon export from source to sink tissues in many plants. Raf plays an important role in the stabilization of membranes during seed desiccation, being accumulated under certain abiotic stress conditions, including heat, cold, salinity, and drought. The first committed step in the pathway of Raf biosynthesis is the reaction catalyzed by galactinol synthase (EC 2.4.1.123), a member of the glycosyltransferase family 8, which produces galactinol from UDP-galactose (UDP-Gal) and *myo*-inositol. Then, raffinose synthase (EC 2.4.1.82) transfers the galactosyl moiety from galactinol to sucrose, thus producing Raf. Several works have shown the relationship of galactinol synthase transcripts with galactinol and Raf levels in response to various types of stressful conditions. However, little is known about the structural, kinetic, and regulatory properties of this enzyme. The present work focuses on galactinol synthase from *Brachypodium distachyon*, a model grass closely related to economically important crops, such as rice and wheat. The gene coding for this enzyme was synthesized *de novo* and the recombinant enzyme was expressed fused to an N-terminal His-tag in *Escherichia coli* cells and purified by IMAC. The activity of *B. distachyon* galactinol synthase was 2-fold higher in presence of Mn^{2+} than with Mg^{2+} , the enzyme exhibiting a 10-fold higher affinity for the former. Enzyme activity in the physiological direction of the reaction (synthesis of galactinol) was optimal at pH values from 7 to 9 and at 35°C. Under standard conditions, the $S_{0.5}$ for UDP-Gal and *myo*-inositol were 0.08 and 2.9 mM, respectively. Interestingly, the recombinant enzyme was inactivated by oxidation with diamide, and the activity was recovered by reduction with DTT, suggesting the existence of a redox regulatory mechanism. A structural model of the enzyme was obtained by protein threading (fold recognition), which was used to determine the residues putatively involved in substrate and metal binding. Overall, our work lays the ground to understand better the synthesis of Raf in plants.

EN-P09

DIFFERENTIAL NADP⁺ BINDING MODE IN BACTERIAL AND PLASTIDIC FERREDOXIN-NADP⁺ REDUCTASES

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Ferredoxin-NADP⁺ reductases (FNRs) constitute a family of monomeric hydrophilic proteins that contain FAD as a prosthetic group. They are classified as either plant- or mitochondrial-type FNRs. Plant-type FNRs are divided into plastidic and bacterial classes. Bacterial FNRs participate in metabolic pathways that are especially appropriate for the development of microbicidal agents because they are not present in humans. Plastidic FNRs have a conserved tyrosine residue at the carboxyl terminus which is interacting with FAD isoalloxazine. This residue would be displaced to allow the entry of NADP⁺. Plastidic FNRs show between 20- and 100-times greater exchange rates than bacterial enzymes. The latter, on the other hand, have a structured variable terminal carboxyl end that has not allowed to propose models justifying how the substrate reaches the active site. The crystallographic structure of bacterial *Escherichia coli* FNR (EcFNR) with the bound nucleotide shows that the NADP⁺ molecule interacts with three arginines (R144, R174, and R184) that would generate a strongly structured site with high affinity for the NADP⁺ substrate. These three amino acids are conserved in other bacterial FNR, but not in the highly efficient plastidic enzymes found in plant chloroplasts and cyanobacteria. The structural alignment of EcFNR with the plastidic *Pisum sativum* FNR (PeaFNR) shows that of these three arginines, only R174 in EcFNR is present in PeaFNR (R229); R144 corresponds to a proline (P199) and R184 to a tyrosine (Y240). We have found NADP⁺ tightly bound to the EcFNR. The bound nucleotide and the structured carboxyl terminus in bacterial enzymes could be the cause of their slower exchange rate. We