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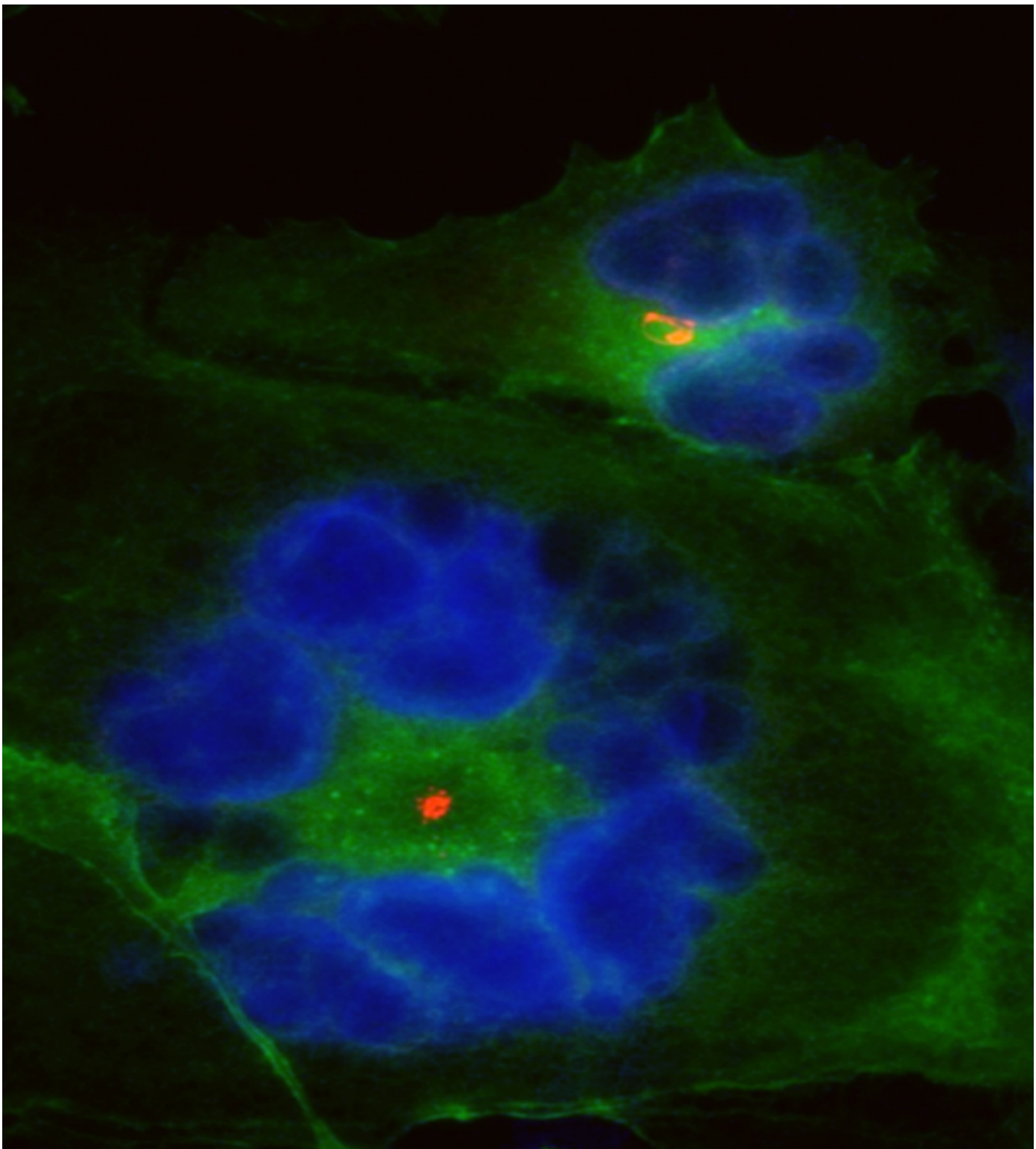

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Cover page: The Synthetic Lethal Rosette

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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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 to1977, 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

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Salmonella is an enteropathogen that causes a wide range of diseases in humans and animals. PhoP/PhoQ is a two-component system (TCS) distributed amongst several Gramnegative bacteria, consisting of the histidine kinase PhoQ, and the transcriptional regulator PhoP. In *Salmonella* Typhimurium, the PhoP/PhoQ system regulates the adaptation to Mg^{2+}-limiting environments and controls key virulence phenotypes such as the invasion and proliferation within host cells. As signal transduction in mammals does not involve TCS, the PhoP/PhoQ system is an attractive target to develop new antimicrobial agents. We have previously reported a methodology based on a TLC-overlay as a new strategy for the search and identification of antimicrobial agents targeting the PhoP/PhoQ system. We applied this bio-guided strategy using a strain carrying a PhoP-controlled reporter gene, to the screening of a dynamic combinatorial library of hydrazones in the search for inhibitors. As a result, two libraries of hydrazones and three libraries of thiocarbazones totaling over 370 members were screened for their inhibitory activity through a rapid inexpensive TLC strategy. Satisfactorily, a complex library of hydrazones that can repress the PhoP/PhoQ system was selected from the initial screening, to further study its members. Through iterative deconvolution of over 100 library members, we identified a potential inhibitor, A25B4. This compound could be synthesized in its pure form, characterized, and it was confirmed that it does not affect the growth of Salmonella. By quantitative β-galactosidase assays, we confirmed its inhibitory activity and it was found that the response was dose-dependent and selective as well. Once the mechanism of action of A25B4 in the system is known, a target protein domain of the TCS will be used to template a library of hydrazones, biasing the composition of the dynamic library towards A25B4. This step will further confirm its affinity and mechanism of action. This strategy allows us to establish a novel methodology for the discovery of the PhoP/PhoQ system inhibitors to fight against *Salmonella*-borne diseases.

PLANTS

PL-C01
CONTRIBUTION OF FLAVODOXIN EXPRESSION IN POTATO PLANTS TO IMPROVED TOLERANCE AGAINST DROUGHT

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Environmental stress represents the most important factor limiting the yield of crops worldwide, a situation that will surely get worse in the near future as a consequence of the deterioration of the global climate. For that reason, numerous strategies have been developed to increase stress tolerance in plants. Within this context, it has been demonstrated that the introduction of a plastid-targeted cyanobacterial flavodoxin (Fld) in transgenic plants resulted in increased tolerance to multiple sources of biotic and abiotic stress. Taking into account these observations and as potato is regarded as the third most important food crop in the world, we generated transgenic potato plants that express Fld in chloroplasts (*Stpfld*) to evaluate their performance under water deficit, which has the highest impact in quantitative terms. We characterized these plants and their wild-type (WT) siblings under hydric stress by interrupting irrigation. We found that negative consequences of water deprivation such as impairment of photosynthesis and increased propagation of reactive oxygen species were detected in WT leaves long before visual symptoms of leaf wilting became apparent, and that these adverse effects were prevented by expression of a plastid-located Fld. These results prompted us to gain further knowledge on the mechanism of tolerance conferred by Fld, therefore a transcriptomic analysis of these plants subjected to drought and control conditions was carried out in potatoes. Water deprivation induced 2529 genes in WT plants against 1697 in *Stpfld*252 siblings and repressed 3172 genes in the wild type versus 2400 in the transformant. Then, the overall effect of Fld presence was to mitigate the changes in gene expression driven by the drought treatment; either induction or repression, suggesting that plants accumulating chloroplast Fld sensed less stress than their WT counterparts. The results showed partial or complete protection of primary metabolisms affected by drought, including the photosynthetic electron transport chain and the Calvin Cycle, indicating that this genetic intervention increases stress tolerance in this species. In addition, these results provide a detailed snapshot of how chloroplast redox biochemistry affects gene expression and metabolism during drought.

PL-C02
NEW ROLES FOR OLD FRIENDS: A MICROTUBULE-LOCALIZED COP1-INTERACTING PROTEIN PROMOTES HYPOCOTYL ELONGATION IN THE DARK

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Plant irritability for light stimuli becomes crucial to cope with ambient fluctuations in order to keep up homeostasis and accomplish the life cycle successfully. Light environment governs plant development. Perception of light is carried out by photoreceptors, such as phytochromes (phyA to phyE) that absorb primarily in red and far-red; and cryptochromes (cry1 to cry3) that are predominantly blue-light receptors. Once perceived, plants are able to integrate light signals into biochemical networks that conduce to proper response. Transducing these light signals involve changes in the phosphorylation state of proteins. In an early light-induced phosphoproteome study in *Arabidopsis thaliana*, we identified a protein that presents light-responsive dephosphorylation in the presence of photoactivated photoreceptors. This protein was particularly interesting because it was reported to interact with the key repressor of photomorphogenesis COP1 and thus, it is potentially involved in early photomorphogenesis

events. *In vivo* assays with a transcriptional reporter revealed it is expressed in cotyledons and elongation zones of hypocotyl and root. Its expression is regulated negatively by light. CRISPR-CAS9 mutated lines exhibit shorter hypocotyls in darkness. Confocal microscopy assays with stably transgenic lines expressing translational reporters revealed localization to cortical microtubules. We are currently studying the biological implications of its microtubule association and its regulation by COP1 through changes in phosphorylation patterns. All these results suggest this protein promotes growth in darkness by affecting microtubules dynamics.

PL-C03
DYNAMIC REGULATION OF CHROMATIN TOPOLOGY BY INVERTED REPEAT-DERIVED SMALL RNAS IN SUNFLOWER

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Transposable elements (TEs) are extremely abundant in complex plant genomes. Small RNAs (siRNAs) of 24 nucleotides in length control its activity in a process that involves *de novo* methylation of targeted loci known as RNA-Dependent DNA Methylation (RdDM). Usually, the epigenetic modifications induced by RdDM trigger nucleosome condensation and a permanent silencing of the affected loci. Here, we show that a TE-derived inverted repeat element (IR), inserted near the sunflower *HaWRKY6* locus dynamically regulates the expression of the encoded gene by altering chromatin topology in different ways. The transcripts of this IR element are processed into 24-nt siRNAs, triggering its DNA methylation together with another two regions of the locus. These epigenetic marks then stabilize the formation of different tissue-specific loops in the chromatin that affect the gene expression in specific ways. In leaves, an intragenic loop is formed, blocking *HaWRKY6* transcription by disrupting the progress of RNA Polymerase II (RNAPII) along the gene. While in cotyledons, the formation of an alternative loop, encompassing the whole *HaWRKY6* gene, enhances transcription of the gene in a phenomenon known as "gene looping" where the RNAPII recycles along the gene. The formation of the latter loop also changes promoter directionality, reducing IR transcription, ultimately releasing the loop. Our results provide evidence that TEs can act as active and dynamic regulatory elements within coding loci in a mechanism that combines RNA silencing, epigenetic modification, and chromatin remodeling machinery.

PL-C04
CONTRIBUTION OF THE DNA GLYCOSYLASE MBD4L TO DNA REPAIR DURING SEED GERMINATION

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DNA repair is crucial to maintain genome integrity and ensure cell survival and accurate transmission of genetic information. Plants experience high levels of DNA damage at different stages of their life, which is often caused by stressful conditions. Cycles of dehydration and rehydration during seed development are associated with high levels of reactive oxygen species, resulting in oxidation of DNA bases and DNA strand breaks. Genome damage is exacerbated during seed aging, decreasing seed vigor and viability. Consequently, DNA must be repaired prior to germination to prevent genomic damage from being fixed after cell division. The base excision repair (BER) contributes to this end by using DNA glycosylases to excise damaged bases from the genome. Here, we studied the expression pattern of the *Arabidopsis* DNA glycosylase MBD4L (methyl-binding domain protein 4 like) during seed development, germination, and seedling establishment. We further analyzed germination phenotypes associated with the deficiency/overexpression of MBD4L. Interestingly, mbd4l mutants showed late germination under basal conditions. This phenotype was not caused by enhanced sensitivity to abscisic acid (ABA). Interestingly, late germination was exacerbated by exposure to genotoxic agents. Therefore, MBD4L may contribute to DNA repair, and consequently to proper plant development, by activating the BER system before seed germination. To test this hypothesis, the expression pattern of MBD4L and genes responding to DNA damaged (LIG1, RAD51, PARP2) has been analyzed along with germination.

PL-C05
EXPRESSION OF NOS ENZYME FROM PHOTOSYNTHETIC MICROORGANISMS IN HIGHER PLANTS: A TOOL TO IMPROVE NITROGEN USE EFFICIENCY

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Nitrogen (N) is one of the major macronutrients for plants. The massive use of N fertilizers in agricultural production has a negative impact on the environment, biodiversity, and human health. The development of strategies to improve the nitrogen use efficiency (NUE) in plants is of relevance in plant biology. Some studies showed that nitric oxide (NO) is a signal for N deficiency in plants as well as a potential source of N since it can be oxidized to $NO3^-$ by phytoglobin. In animals, the enzyme NO synthase (NOS) catalyzes the biosynthesis of NO from the arginine substrate. Some evidence suggests the existence of a putative NOS activity in plants; however, NOS sequences were not found in land plant genomes. In recent years, NOS enzymes were identified in photosynthetic microorganisms such as green algae, diatoms, and cyanobacteria. In our lab, the functionality of the NOS from the cyanobacteria *Synechococcus* PCC 7335 (SyNOS) was characterized. SyNOS has a similar structure to animal NOS with both oxygenase and reductase domains and contains an additional domain in the N terminus that encodes to a globin. It has been demonstrated that the globin domain of SyNOS acts as a NO dioxygenase, oxidizing NO to $NO3^-$. As a result, SyNOS is able not only to produce