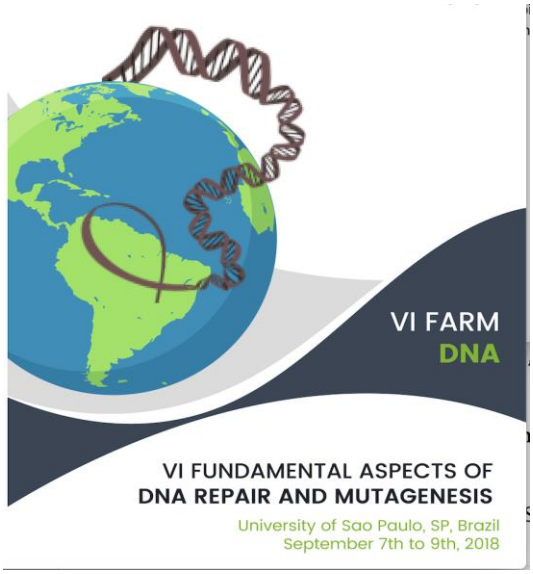

Special GMB issue for the 6th FARM DNA (Fundamental Aspects of DNA Repair and Mutagenesis) meeting.

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The FARM-DNA meetings aim to promote the area of DNA repair and mutagenesis science in Brazil, by encouraging the interaction between scientists and students working on various aspects of these subjects. The sixth edition occurred in São Paulo, SP, at the University of São Paulo, from September 7th to 9th, 2018, as a satellite event to the International Congress of Genetics, in Foz do Iguaçu, PR, Brazil. As indicated by their title (FARM DNA meeting), these meetings would like to act as seeders, planting in students and young investigators the interest in learning and investigating the mechanisms used by cells to maintain genomic stability. Several renowned scientists participated, which led to profound discussions on fundamental scientific questions at the frontiers of our understanding of how genomes suffer damage, the repair processes that warrant genome stability, and the main consequences of unrepaired DNA lesions for cells (such as chromosomal instability, mutations, and cell death) as well as for the whole organism (such as cancer and aging). Importantly, the meeting was particularly geared toward motivating students and advance their expertise, especially through peer interaction.

The 6th FARM-DNA attracted more than 180 participants and covered many different topics on the subject. We are very happy to report that, for the first time, we now had the opportunity to assemble all the excitement of the meeting in a special issue dedicated to the FARM-DNA meeting, published in the open access journal Genetics and Molecular Biology in the form of 14 review and original research articles. All the special issue articles can be accessed at the journal's webpage via the SciELO platform: (https://www.scielo.br/scielo.php?script=sci_issuetoc&pid=1415-475720200002&lng=en&nrm=iso).

Among the articles, several focused on DNA repair mechanisms and DNA damage responses (DDR). Cussiol et al. (2020) present a historical perspective on the discovery of kinases that participate in DDR, initially in yeast, and how this knowledge contributed to the discovery of the functions of their orthologs in mammalian cells. Additionally, Munoz et al (2020) presents a review discussing how DDR, mainly due to these kinases, modulate the alternative splicing process in human cells, adding a novel level of complexity to the cellular responses to DNA damage.

The Gottifredi group (Paviolo et al, 2020) presents new scientific data obtained in an isogenic cell line model, indicating that the synthetic lethality promoted by Olaparib (a poly (adenosine diphosphate (ADP)-ribosyl) polymerase, PARP, inhibitor) in BRCA deficient cells results in fact in genotoxic stress and genomic instability, as previously described. However, contrary to the previous hypothesis, BRCA mutated cells do not display persistent accumulation of double strand breaks that precede cell death. Also reviewed are the mechanisms of PARP-promoted post-translation modifications under DNA damage conditions in human cells, and how this knowledge is opening therapeutic perspectives for human diseases, such as cancer, ischemic damage, and neurodegeneration (Hoch and Polo, 2020). Kumar, Moreno et al (2020) reviewed recent findings on the interplay between two distinct mechanisms, base and nucleotide excision repair (known as BER and NER, respectively), and how they exchange and cooperate to remove specific DNA lesions.

Other articles discuss how DNA damage and genomic stability are directly related to the development of tumor cells. Primo and Teixeira (2020) discuss how oncogene activation, a normal phenomenon in many tumor cells, may result in DNA replication stress and how this contributes to genome instability in human cells. The Valente group (Souza et al, 2020) discusses the potential roles of a DNA repair network

helping glioblastoma cells to manage DNA damage and replicative stress, contributing to therapeutic resistance in these tumors. Faria and Fortunato (2020) discuss the structure and physiological functions of the NOX/DUOX family of enzymes that generate radical oxidative species in human cells, and their potential roles in cancer biology.

The stability of the mitochondrial genome is also addressed in this special issue. Oliveira et al (2020) proposes and discusses potential mechanisms that could implicate the mitochondrial replisome, including DNA polymerase gamma and the helicase Twinkle, in originating mitochondrial DNA (mtDNA) deletions, normally found in human mitochondrial diseases. Human mitochondrial diseases are also discussed by Chiaratti et al (2020), focusing on the basic aspects of maternal mitochondrial DNA inheritance in mammals. Mori and Souza-Pinto (2020) investigate how mutations in the *XPC* gene (that encodes one of the NER proteins) affect the expression of the transcriptional co-activator PGC-1α. They obtained data that indicate that both PGC-1α and PPRC1 proteins cooperate in mitochondrial biogenesis and maintenance in dermal fibroblasts, as opposed to other cell types.

Another aspect that was discussed are human genetic diseases that are defective in DNA repair processes. Vessoni et al (2020) review the main research and the attempts to understand the complex phenotype of the human genetic disease Cockayne syndrome (CS). CS combines progeria-like features and developmental abnormalities, and is caused by deficiencies in repair of DNA lesions in transcriptionally active genes. On the other hand, the interesting history of a community of Anjouan, a Comorian island in the Indian Ocean, is revisited due to the high frequency of xeroderma pigmentosum (XP) patients (mutated in the XPC gene, that participates in NER). The haplogroup containing this founder "Comorian mutation" was found to be of Bantu origin and probably originated in the African continent. Genetic and historical data led to the proposal that the inhabitants of Anjouan hid deep in that island to avoid slavery through the hands of the Arabs, who arrived on the island during the 11-13th centuries (Sarasin et al, 2020).

Finally, Repoles et al (2020) present a comprehensive discussion on how the infection of the parasite *Trypanosoma cruzi* (causative agent for the human Chagas' disease) in human cells may result in oxidative stress that damages the genome and elicits DDR in both parasite and host cells.

We hope that this special issue will draw your interest and help you to understand how studies on genome stability can promote the understanding of different aspects of cell biology, as well as contribute directly to human health in many different ways. Enjoy the reading.

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