PLENARY SESSION 2: New avenues for target discovery

O2.1

No abstract available

O2.2

Chromatin dynamics – epigenetic parameters and cellular fate

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Chromatin organization in the nucleus provides a large repertoire of information in addition to that encoded genetically. A major goal for my group involves understanding how histones, the major protein components of chromatin, the bricks, can mark functional regions of the genome through their variants or post-translational modifications, along with non-coding RNA and other chromatin regulators. Errors in the establishment and propagation of these chromatin components, possibly involving imbalance in their deposition pathways, can lead to mis-regulation of genome functions and pathological outcomes, such as cancer. The propagation of centromeric identity represents a model of choice for the study of epigenetic mechanisms. Our work has focused on histone chaperones, as architects of chromatin organisation. We will present our latest findings.

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O2.3

DNA damage response pathway inhibition – a pipeline and the phase 1 experience

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Damage to DNA in humans is constantly occurring, is variable, and depends on inherent cell DNA stability and the environmental conditions that induce DNA damage. DNA damage events can happen at a rate between 1,000 and 10,000 damage events per cell per day, depending on species, requiring sophisticated mechanisms to recognize and repair the multitude of different damage types. Aberrations in DNA damage and repair pathways are even more frequent in cancer cells, and the DNA damage response (DDR) has emerged as an

attractive intervention point for the development of new molecules for the treatment of cancer. New insight into DDR mechanisms has allowed a number of new druggable targets to be identified. We are developing a number of DDR small molecule inhibitors targeting different components of the DDR, such as DNA-PK, ATM, and ATR. An overview of their development, of the approach taken to define a biologically efficacious dose, and of the experience in their development will be presented.