# Abstracts
# E3 - Genomics and Epigenetics

**E3-1**

## Mechanistic insights into the transcriptional arrest in the presence of Double Strand Breaks

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Double-strand breaks (DSBs) occur frequently in the genome during genome replication or by DNA damaging agents. DNA lesions affect fundamental DNA-dependent nuclear processes, such as replication and transcription. We have developed an experimental system where DSBs are induced at coding regions of RNA polymerase II transcribing genes. We have started to study the kinetics of RNA polymerase II transcription inhibition in the presence of DNA breaks. We observed that induction of the break led to transcription inhibition and the restoration of transcription closely followed the dynamics of the repair of breaks. We confirmed by chromatin-immunoprecipitation that the break induction led to displacement of RNA polymerase II affecting both the elongation and the initiation of transcription. Our results show that this is dependent on one of the major kinase in DNA damage repair called DNAPKcs. We also investigated the downstream steps of RNA polymerase II removal and we claimed that it was a multistep process involving additional kinases and ubiquitin ligases NEDD4 and CUL3. At the last step of break dependent transcriptional silencing the RNA polymerase II is targeted for proteasome dependent degradation. These data demonstrate that the DNA damage repair complexes and proteasomal system have a synergistic and active role in transcriptional silencing during the DSB repair by removing the RNA pol II from the transcribing region. We show here that DNA lesions occurring at transcribed regions cause a transient repression until the lesion is repaired. This is probably a cell defense mechanism to avoid production of truncated or mutated transcripts in essential genes whose alterations in their gene expression would endanger cell viability. Understudying the role of DNAPKcs, in preventing RNA pol II bypassing a DSB might be a key in avoiding the production of mutated transcripts that could lead to cancerous phenotypes.

**E3-2**

## Transcriptional Interference Networks

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Earlier we proposed the existence of a previously unrecognized layer of genetic regulation termed transcriptional interference networks (TINs), which is based on the interplay between the adjacent genes through their transcriptional machineries. TINs are essential genetic units, which are assumed to be especially important in processes exhibiting a definite time course of gene expressions, such as embryonic development, tissue regeneration, response to external stimuli, metabolism, viral life cycle etc. The function of TINs is supposed to coordinate the switch between the ON and OFF states of the interacting genes, as well as to reduce the transcriptional noise. Furthermore, TINs simplify the regulation of genes, because they diminish the need for the change in the composition and/or the chemical modifications of the transcription factors. The operation of TINs is demonstrated by the analysis of gene expression and genomic organization of pseudorabies virus, a neurotropic herpesvirus. The transcriptome of the virus has been analyzed using real-time RT-PCR, as well as Illumina HiScan and PacBio RSII platforms. Additionally, we have developed a mathematical approach based on graph-based modeling of the TINs.