



University  
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Department  
Biozentrum



Swiss Institute of  
Bioinformatics

BIOZENTRUM

The Center for  
Molecular Life Sciences

Basel Computational Biology Seminar:  
22830-01 Current Research in Bioinformatics I

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## Decoding the origins of mutations: From tumor signatures to germline hotspots

Mutations record the history of DNA damage and repair across both somatic and germline lineages. I will present two studies that uncover new principles of mutational patterning. First, I will introduce SigNet, a neural network-based method for decomposing mutational signatures in cancer genomes. By learning correlations among mutational processes, SigNet enables accurate inference even from sparse data. Using this approach, we identify associations between tumor hypoxia and multiple mutational signatures and shed light on the elusive determinants of “clock-like” mutational processes, which still remain poorly understood despite their universal activity. In the second part, I will turn to the human germline, where we identify a mutational hotspot at transcription start sites. We trace this hotspot to early embryonic mosaicism and show its association with transcription-related DNA damage and alternative double-strand break repair, implicating a recombination-independent mechanism. Genes affected by this process are enriched for cancer and neurological phenotypes, highlighting its biomedical and evolutionary significance.

**Date:** Monday, November 24, 2025

**Time:** 16:15 h – 17:30h

**Location:** Biozentrum, 02.073

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