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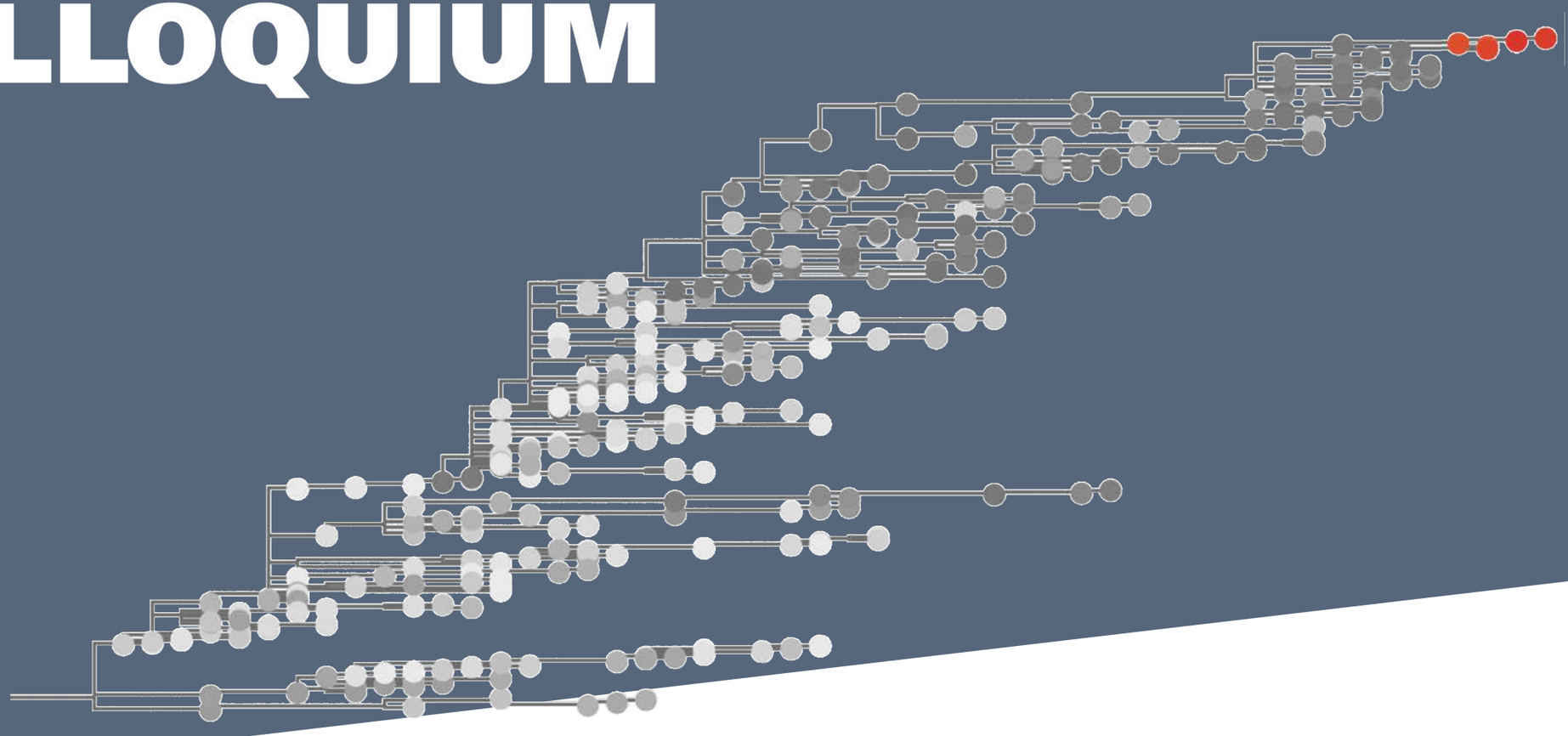

The evolutionary dynamics of healthy and pre-cancerous human blood

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Cancer is a disease of evolution. The first mutational steps in this evolutionary process begin years before the development of cancer. This raises the possibility that these early events could be used as a bellwether for predicting who is most at risk of developing cancer in the future and possibly to intervene. Blood provides an ideal model tissue to study this because of its ease of serial sampling and its relative lack of spatial structure.

In this talk I will present a simple population genetic and evolutionary framework that analyses mutations found in the blood of ~50,000 healthy individuals to identify which mutations confer the largest fitness advantages. This framework reveals that positive selection, not drift, is the major force shaping somatic evolution in healthy blood and that the remarkably wide variation in variant allele frequencies observed across individuals is largely driven by chance differences in the timing of mutation acquisition combined with differences in the cell-intrinsic fitness effect of variants. Extending this framework to account for mutation co-occurrence, we show how synonymous variants provide evidence that most clonal expansions in healthy blood are driven by “unseen” mutations often not covered in cancer-gene panels. Finally I will describe on-going work in our lab exploiting a remarkable collection of serial blood samples which, combined with error-correctable DNA sequencing, enables us to "rewind time" and see how blood cancer evolves from healthy tissue over decade-long timescales.

Wednesday, June 24, 2020,17:00
University of Cologne
Online via Zoom

Hosted by Fernanda Pinheiro and Michael Lässig

CRC 1310 PREDICTABILITY IN EVOLUTION