Inheritance entropy: A model-independent method to probe the hereditary structure of cell lineage trees

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Quantifying the impact of hereditary transmission within lineage trees remains a fundamental challenge universal to a wide array of biological domains. In this talk, I will introduce and discuss the new concept of inheritance entropy, a quantity designed to gauge the hereditary structure of inactive cells across a lineage. We measured this entropy in 32 human stem cell clonal colonies, obtained from high-definition single-cell lineage tracing experiments, and showed that in the greatest majority of clones the entropy is decisively smaller than that of the corresponding non-hereditary ensemble, hence proving that variations in the proliferative power of stem cell lineages are determined by hereditary epigenetic factors that regulate cell-cycle exit. The method can also be employed to locate the specific node of the tree where a mutation in the probability of inactivity occurs, together with a determination of the lag between the mutation ultimately leading to inactivity and its actual expression. This framework can be used to assess in a robust, simple and model-agnostic way the hereditary origin of differential growth in any type of lineage trees.