

ATLAS- Development of laser-based technologies and prototype instruments for genome-wide chromatin immunoprecipitation analyses

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Deciphering the complexity of chromatin-encoded information is the prerequisite for understanding the regulatory circuits governing development and (patho)physiology. Transcription factors and epigenetic modulators translate chromatin-embedded information in a dynamic and cell/gene context specific manner to orchestrate homeostasis, growth and differentiation. To date, the most powerful and commonly used approach is immunoprecipitation of chemically cross-linked chromatin (XChIP) coupled with single gene or global analysis using DNA tiling arrays (ChIP-chip) or parallel single molecule sequencing (ChIP-seq).

At present, serious limitations of the XChIP technology preclude factor-DNA interaction studies at dynamic ranges below minutes. Moreover, conventional XChIP cannot be used to study samples of <10⁶ cells or cell populations within complex biological samples. Based on established proof-of-principle experiments, the multidisciplinary ATLAS consortium will develop novel types of femtosecond (fs) UV tunable lasers to induce highly efficient DNA-protein crosslinking for ChIP analyses with unprecedented precision and reproducibility, and extending the present dynamic time range by order of magnitudes. ATLAS will further validate LaserChIP (LChIP) technologies and integrate them e.g. with manipulation of irradiated (frozen) tissues slices and microfluidic cell sorting systems.

Combining LChIP with proximity ligation approaches will facilitate the analyses of cell-selective (epi)genetic programs on small pre-defined cell populations down to the single cell level. Integration of innovative SMEs with physicists, oncologists, biologists, chemists and mathematicians secures efficient introduction and application of LChIP in basic and translational research. This consortium has the technical and commercial expertise as well as the capacities to successfully develop and commercialize laser-based ChIP technologies.

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