Dynamic changes of histone H3 marks during Caenorhabditis elegans lifecycle revealed by middle-down proteomics - DTU Orbit (08/11/2017)

Dynamic changes of histone H3 marks during Caenorhabditis elegans lifecycle revealed by middle-down proteomics

We applied a middle-down proteomics strategy for large scale protein analysis during in vivo development of Caenorhabditis elegans. We characterized post-translational modifications (PTMs) on histone H3 N-terminal tails at eight time points during the C. elegans lifecycle, including embryo, larval stages (L1 to L4), dauer and L1/L4 post dauer. Histones were analyzed by our optimized middle-down protein sequencing platform using high mass accuracy tandem mass spectrometry. This allows quantification of intact histone tails and detailed characterization of distinct histone tails carrying co-occurring PTMs. We measured temporally distinct combinatorial PTM profiles during C. elegans development. We show that the doubly modified form H3K23me3K27me3, which is rare or non-existent in mammals, is the most abundant PTM in all stages of C. elegans lifecycle. The abundance of H3K23me3 increased during development and it was mutually exclusive of the active marks H3K18ac, R26me1 and R40me1, suggesting a role for H3K23me3 in silent chromatin. We observed distinct PTM profiles for normal L1 larvae and for L1-post dauer larvae, or L4 and L4 post-dauer, suggesting that histone PTMs mediate an epigenetic memory that is transmitted during dauer formation. Collectively, our data describe the dynamics of histone H3 combinatorial code during C. elegans lifecycle and demonstrate the feasibility of using middle-down proteomics to study in vivo development of multicellular organisms. This article is protected by copyright. All rights reserved.

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