composite microstructure of the building units, which we imaged by EBSD down to the submicron scale and which is essential for the mechanical strength and self-sharpening ability of the calcite teeth. There is direct as well as indirect evidence supporting the paradigm [6] that most if not all of the biocalcites grow from amorphous precursors. Crystallographic textures vary from weakly cylindrical (in coralline red algea) via the very frequent strongly cylindrical textures in shell valves to 3-dimensional single crystal-like coherence.

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Keywords: biomineralisation, microstructure, texture

MS.15.1

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Structural and functional analysis of the ISW1a chromatin remodeling complex

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Saccharomyces cerevisiae (Yeast) ISW1a is classified into the Imitation Switch (ISWI) subgroup of the ATP-dependent chromatin remodeler superfamily including the SWI2/SNF2-, CHD1- and INO80-subgroups, each with various chromosomal processing activities. The main function of ISW1a is the repression of gene expression by an ATP-dependent modulation of nucleosome positioning around the promoter region. ISW1a is comprised of two subunits, Isw1 and Ioc3, with a total mass of 220 kDa. Isw1 contains the N-terminal ATPase domain of 633 amino acids as its catalytic motor domain connected by a linker of 133 amino acids to the C-terminal domain composed of three consecutive subdomains (Hand, Sant and Slide: "HSS"). This HSS region, comprising 300 amino acids, has been shown by many biochemical studies to be the DNA binding module of Isw1. The Ioc3 subunit is composed of 787 amino acids and has a significant amino acid similarity to yeast Esc8, which is implicated in gene silencing. Ioc3 is as yet poorly characterized, with only one biochemical study suggesting it to be a general DNA binding protein. Its domain composition and structure are entirely unknown. Here we present the crystal structures of ISW1a lacking the ATPase domain (ΔATPase) as a HSS-Ioc3 complex, either without DNA (resolution 3.25Å) or with two DNA segments bound independently to Ioc3 and HSS (resolution 3.6 Å). The structures reveal four fundamental aspects for the ISWIa complex. (1) The complex is 'L'-shaped (approximately 130 x 80 x 60 Å) with a large, tight interface between HSS and Ioc3 (buried surface area 5303 Å^2). (2) The novel protein fold architecture of Ioc3 has two major protruding subdomains: a domain composed entirely of loops functionally involved with the Sant subdomain interaction, and a domain containing a five-helix bundle potentially involved in nucleosome recognition. (3) Ioc3 has a novel recognition motif and binds the major groove of DNA with some sequence specificity. This motif is formed from two loops originating from two widely separated regions of the primary sequence. (4) Sant and Slide are structurally similar subdomains, each composed of three-helix bundles. Together the two subdomains bind a second copy of DNA, but in a topologically unique manner: the first helix of Sant lies across the DNA minor groove while with Slide the third helix contacts the DNA and is aligned parallel to the minor groove. Neither of these interactions shows any sequence specificity.

In further studies, EM analysis of a complex of ISW1a with a nucleosome revealed two forms of HSS-Ioc3-mononucleosome complexes. By interpreting the cryo-EM 3D images of these two complexes on the basis of our atomic-resolution structures of the nucleosome core particle and of the HSS-Ioc3-DNA complex, it was apparent that the HSS-Ioc3 complex had opposite orientations with respect to the nucleosome in the two forms (with either the Hand subdomain or Ioc3 bound to the nucleosome). These two structures can be integrated into a model with one HSS-Ioc3 complex located on linker DNA between two adjacent nucleosomes (a di-nucleosome). Using biochemical mobility assays with ISW1a (with ATPase) complexed with a di-nucleosome, we have shown that the ATPase domain of ISW1a drives the uni-directional relocation of the DNA wrapped around a nucleosome. Taken together, our data allows us to describe the entire remodeling mechanism of ISW1a for nucleosomes in the higher order chromatin structure.

Keywords: chromatin, nucleosome, structure

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Combinatorial readout of histone H3 modifications specifies localization of ATRX to heterochromatin

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Accurate read-out of chromatin modifications is essential for eukaryotic life. Mutations in the X-linked ATRX gene cause a mental retardation syndrome [1], while wild-type ATRX protein targets pericentric and telomeric heterochromatin for deposition of the histone variant H3.3 [2] via a largely unknown mechanism. Here, we show that the ADD domain of ATRX, where most syndrome-causing mutations occur, engages the N-terminal tail of histone H3 through two rigidly oriented binding pockets, one for unmodified Lys4, the other trimethylated Lys9. *In vivo* experiments show that this combinatorial readout is required for ATRX localization, with recruitment enhanced by a third interaction via heterochromatin protein 1 (HP1) that also recognizes trimethylated Lys9. The cooperation of ATRX ADD domain and HP1 in chromatin recruitment results in a tripartite interaction that may span neighbouring nucleosomes and illustrates how the "histone-code" is interpreted by a combination of multivalent effector-chromatin interactions.

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Molecular mimicry in the assembly of chromatin protein complexes

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