Importance of Histone Acetyltransferase 1 as a novel acyl transferase Sonya Staneva, Iva Ugrinova, Saadi Khochbin

Histone acetyltransferase 1 (HAT1) is an enzyme that acetylates newly synthesized histones H3 and H4 after they are translated in the cytoplasm and prior to their nuclear localization. Its activity towards free histone H4 is highly conserved throughout eukaryotic evolution and, with acetylation being always mediated at the same positions – lysines 5 and 12 on the NH2-terminal tail. All the acetylations achieved by HAT1 are rapidly removed upon nucleosome assembly and numerous studies have proven that they are not necessary for nuclear localisation nor for chromatin assembly. We constructed a working hypothesis based on recent papers and our own unpublished data in order to investigate the role of HAT1 and its' importance for histone dosage, stability, turnover and degradation having in mind its' potential ability to mediate not only acetylation but other post-translational modifications (acylations). For this purpose, we performed HAT1 knockdown in a model cell line and observed how silencing the expression of this enzyme would affect its different functions. We concluded that:

1. HAT1 is not important for the total histone concentration in the cell.

2. HAT1 – specific acetylations remain unchanged upon knockdown

3. HAT1 is not a main chromatin histone acetyltransferase.

4. HAT1 is a novel acyl transferase that can mediate different types of post-translational modifications both on histones and non-histones proteins.