Histonas y regulación de la expresión génica en *Candida. albicans*
Histones and regulation of gene expression in Candida albicans
Ángel Domínguez Department of Microbiology and Genetics, CIETUS, IMB, University of Salamanca. e-mail: ado@usal.es

The availability of whole-genome sequences and advances in microarray technologies have greatly advanced our understanding of chromosome organization and gene transcription. However, the chromosomal context of a DNA sequence is crucial to its transcriptional activity because of the regulatory effects of the main DNA-packaging proteins, the core histones. The core histones, H2A, H2B, H3 and H4, form an octameric complex, around which 147 bp of DNA are wrapped to form the nucleosome, which packages chromatin and is a general repressor of transcription. The properties of histones, and therefore nucleosomes, can be altered by the post-translational addition of small chemical modifications, such as acetyl, methyl, phosphoryl, ubiquityl and sumo groups, to regulate diverse processes that include gene activity, gene silencing by heterochromatin, replication of DNA, apoptosis and responses to DNA damage. As histones can be modified at several amino-acid residues, an attractive hypothesis is that there are combinations of histone modifications at specific genetic loci that lead to discrete biological outcomes — for example, a combination of modified and unmodified acetylation sites at the promoter of a gene could lead to transcriptional activation. Histone acetylation is mediated partly by the recruitment of specific histone acetyltransferases (HATs) and deacetylases (HDACs) to genomic loci by transcription factors, resulting in modulation of gene expression. Although several specific interactions between transcription factors and HATs and HDACs have been elaborated in several eukaryotic systems, including *Saccharomyces cerevisiae*, the full regulatory network remains uncharacterized. We are interested in the HAT complexes containing the Gcn5p; -the Gcn5p-SAGA complex (Spt-Ada-Gcn5-acetyltranferase) and the ADA (Ada2-Gcn5-Ada3) that acetylate histones H3 and H2B and NuB4 complexes (formed by Hat1p, Hat2p and Hif1p) nuclear type B histone acetyltransferase specific for histone H4. Looking to HDACs we are specifically interested in Rpd3p, Hos2p and Hos1p (class I HAD) and in Hda1p and Hos3p (class II) and in the *SIN3* gene which codes for a co-repressor. We have deleted all this genes in *C. albicans* and none of them are lethal. All deleted strains show at least a variation in the solid phenotype when comparing with the reference strain, but in liquid media most of them present a similar phenotype to the wild type. Double mutants are also viable. The most drastic phenotype is shown by the *sin3* and *gcn5* mutants. We have carried out transcriptome analysis of all of the mutants growing either as yeast or during the yeast-hypha transition (at 15 min. 1 and 3 hours). *SIN3* and *GCN5* genes regulate the highest number of genes. *HAT1* and *HAT2* genes appeared to regulate different set of genes and do not show additive effects when we analyze the double mutant *hat1, hat2.* Our results suggest that also that the NuB4 complex only act in the nucleus. Finally disruption of *HOS2* gene produces a change in the metabolism inducing the glyoxylate cycle.