

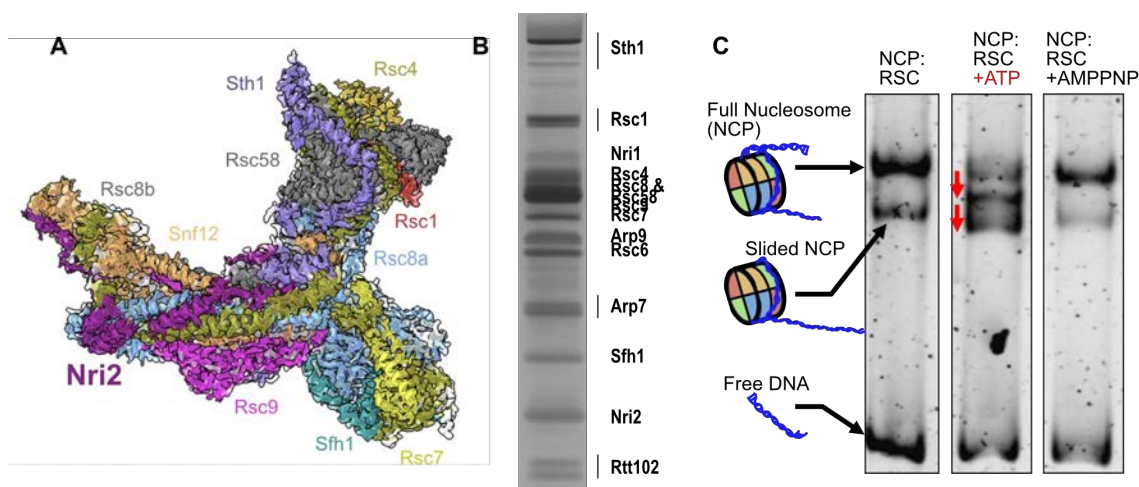
## Structural study of the chromatin remodelling complex RSC in *Candida albicans*.

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Candidiasis is a fungal infection caused by fungi of the genus *Candida*, of which *C. albicans* is the main culprit. Invasive fungal infections are responsible of approximately 3.8 million deaths per year [1]. The RSC complex (Remodeller of the Structure of the Chromatin) is well studied in *S. cerevisiae*. This remodeller, from SWI/SNF family, moves nucleosomes to -1 or +1 of the transcription start site (TSS) [2]. It is essential for eukaryotes and promotes gene expression in nucleosome-depleted regions. The resolved structures of *S. cerevisiae* 16-subunits complex (ScRSC) have made it possible to highlight the architecture of this remodelling complex in fungi [3]. However, mass spectrometry analyses indicate a 14-subunits composition of *C. albicans* complex (CaRSC). Three subunits from *S. cerevisiae* (Rsc3, Rsc30, Ldb7) do not have homologs in *C. albicans*. Moreover, two novel subunits (*Nri1* and *Nri2*) had been found but their function remained unknown [4]. Here we have used cryoEM to solve the structure of the *C. albicans* 11-proteins-core-endogenous-RSC-complex at a 3Å resolution. We also validated its 14-subunits composition and its activity. We revealed most of *Nri2* structure within the RSC complex. This mysterious subunit seems to be structurally homologous to human SMARCE1 and *S. cerevisiae* Htl1. This protein is not oriented towards the nucleosome and has no remarkable domain of activity. Repressive conditional mutants of the *NRI2* gene (TetOFF) validate its role in yeast growth at high temperatures. *Nri2*, Htl1 and SMARCE1 belong to a class of stabilizing proteins whose role is to maintain the structure of polybromodomain complexes of the SWI/SNF family. Using our low-resolution density map and AlphaFold 3 presets, we predict the interaction of *Nri1* with the tail of the complex at Rsc9. We develop pull-down assay on recombinants Rsc9 and *Nri1* but *Nri1* role remains unknown.



**Figure 1.** Structure Composition and activity of the RSC complex in candida albicans. A/ CryoEM-resolved structure of the core complex at 3Å resolution. Subunits are shown in different colors. B/ SDS PAGE illustrating the subunits of the purified complex. C/ EMSA showing the activity of the complex on nucleosomes. In the presence of its substrate (ATP), there is a shift in nucleosome migration.

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