

## Soutenance de thèse

## Functional study of human RNA Polymerase III specific subunits hRPC62 and hRPC39.



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In eukaryotes, nuclear transcription is carried out by DNA dependent RNA polymerases (Pol) I, II and III. Pol I transcribes ribosomal RNA's, Pol II produces essentially messenger and micro RNA's whereas Pol III transcribes small untranslated RNA's involved in a variety of cellular processes such as translation, splicing or the regulation of transcription. Human Pol III is a multi-subunit enzyme composed of 17 subunits. The majority of these subunits are homologous or closely related to Pol II and/or Pol I subunits. However, five subunits are specific to Pol III with no counterparts in Pol I or Pol II. One of the Pol III specific subunits, hRPC32 has two paralogues,  $\alpha$  and  $\beta$ , expressed from two different genes. hRPC32 $\beta$  is expressed ubiquitously while hRPC32 $\alpha$  or  $\beta$  associate with two other Pol III specific subunits, hRPC62 and hRPC39, to form stable ternary sub-complexes thought to be implicated in transcription initiation. The purpose of this work was to clarify the functional mechanism of hRPC32 $\alpha/\beta$ -hRPC62-hRPC39 sub-complexes.

In this study, we first mapped the protein-protein interaction of hRPC62 with hRPC32 $\alpha$  and hRPC32 $\beta$ . In addition, we analyzed biochemical and functional properties of hRPC62 and hRPC39. We also investigated functional similarities between hRPC62 and TFIIE $\alpha$ , a Pol II general transcription factor shown to have structural similarities with hRPC62. Our data offer a new vision of Pol III transcription with respect to its mechanism and its implication in various cellular processes.