The Role of Human Nip7 Ortholog (HSNIP7) in pre-rRNA Processing of Human Cells.

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Eukaryotic ribosome is best characterized in the yeast. However, the association of several human genetic syndromes with loss of function in genes encoding proteins related to ribosome synthesis and function has brought new attention to pre-rRNA processing and ribosome biogenesis in human cells. One of such syndromes, SBDS (Shwachman-Bodian-Diamond syndrome) is caused by a mutation in the SBDS gene which encodes a protein involved in ribosome biogenesis. In a previous work, we showed that SBDS is found in complexes containing the human Nip7 ortholog, HsNip7. Yeast Nip7p functions in pre-rRNA processing and interacts with Rrp43p, a subunit of the exosome. The HsNip7 function on pre-rRNA processing in human cells was investigated by using HEK293 cells knock down for HsNip7 obtained by using RNA interference. Northern blot analysis of stable HsNip7 knock down HEK293 derivatives cells revealed a global pre-rRNA processing deficiency, with a significant delay in processing at site 1. Among the defects are accumulation of A'→2 and A0→2c aberrant precursors and reduction of the 37S and 34S precursors of the 18S pathway and, reduction of the 32S precursor of the 28S pathway. In addition, a new fragment of the ITS2 region was identified suggesting a second endonucleolytic processing site downstream the 3' end of the 5.8S rRNA. Primer extension assays were used to determine the 5' end of the rRNA 18S. This analysis corroborates northern blot results, showing reduction of processing site 1. These results indicate that HsNip7 deficiency affects mainly 18S rRNA maturation in human cells.

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