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The G-patch protein Tma23 is a novel Prp43 cofactor involved in early pre-60S subunit assembly

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Ribosomes are molecular machines that are highly conserved across all three domains of life. In eukaryotes, ribosomes are composed of four ribosomal RNAs and ~80 ribosomal proteins, which are assembled into two structurally and functionally distinct ribosomal subunits: the small 40S and the large 60S subunit. Ribosome biogenesis is an intricate and highly energy-demanding process, which requires the coordinated action of more than 200 assembly factors and ~75 small nucleolar ribonucleoprotein particles (snoRNPs). Extensive research in the field of ribosome biogenesis, mainly employing the yeast *Saccharomyces cerevisiae* as a model organism, has enabled to obtain a detailed view of the cascade of assembly and maturation events that lead to the formation of mature ribosomal subunits. Nevertheless, partly owing to the lack of structural information, the initial steps of 60S subunit assembly are still far from being fully understood.

The first 60S intermediate for which structural information is available notably contains the assembly factor Nsa1. Here, besides revealing additional mutations in Nop1, Nop4, Mak5, and Ebp2, we identified changes within the coding sequences of Noc1, Nop12, Prp43, Tma23, Bcd1, components of the box C/D snoRNP U24, and the ribosomal proteins uL4 and uL30, as novel suppressor mutations that bypass the requirement for the essential protein Nsa1. Remarkably, we could unveil that the G-patch domain-containing Tma23 physically interacts with the DEAH-box RNA helicase Prp43. Furthermore, we provide experimental evidence supporting that Tma23 is implicated in early nucleolar pre-60S assembly. Interestingly, Tma23 displays overall similarity to Pxr1, a well-established Prp43 cofactor, and we show that Tma23 and Pxr1 physically interact and that their function appears to be required for the correct maturation and functionality of box C/D snoRNPs. We speculate that, by assisting maturation or ensuring proper functionality of box C/D snoRNPs, Tma23, Pxr1, and Prp43 might contribute to the initial formation of pre-60S ribosomes.

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