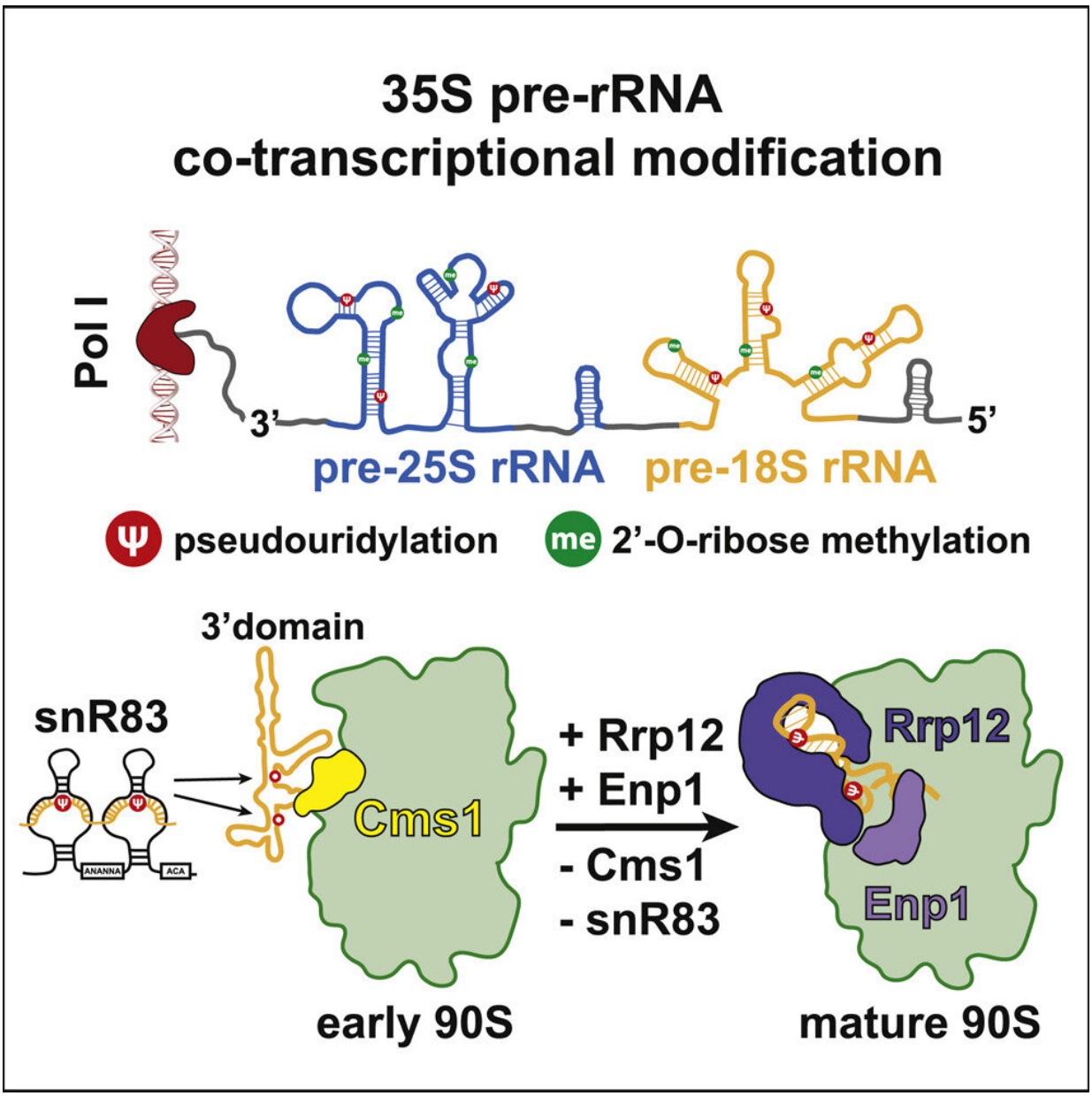
Decoding the special role of a biogenesis factor in the maturation of precursor ribosomes

February 8 2023, by Marietta Fuhrmann-Koch



Graphical abstract. Credit: *Cell Reports* (2022). DOI: 10.1016/j.celrep.2022.111684

Ribosomes are the nanomachines of the cell whose task is the correct synthesis of proteins. Researchers at the Heidelberg University Biochemistry Center are studying the emergence of these "protein factories", also known as ribosomes.

Led by Prof. Dr. Ed Hurt, they have decoded the special role of a heretofore unexplored biogenesis factor in the maturation of precursor ribosomes. The research results, obtained in close cooperation with colleagues of Ludwig Maximilian University of Munich, were published in the journal *Cell Reports*.

Every cell has a number of these nanomachines that act as protein factories manufacturing vital proteins with various tasks for the organism. A functional ribosome consists of two subunits that are assembled during formation by helper proteins—so-called biogenesis factors. The ribonucleic acids (RNA) and proteins are united into precursors and later complete ribosomes. This process begins in the cell nucleus with the manufacture of a long RNA chain.

Step by step, the chain is biochemically altered at selected RNA modules, whereby short RNA molecules known as snoRNAs—small nucleolar RNAs—guide the required enzymes to the selected RNA bases. The precursor RNA chain is then trimmed and finally embellished with ribosomal proteins. "Until now it was unclear when the individual modules are modified and how these modifications are coupled with other maturation steps," explains Ed Hurt, Senior Professor at the

Heidelberg University Biochemistry Center (BZH).

Working with researchers at the Gene Center of Ludwig Maximilian University of Munich, the Heidelberg scientists were able to demonstrate how a previously unstudied biogenesis factor called Cms1 temporally coordinates the maturation of precursor ribosomes. A highly specific, local chemical change in the ribosomal RNA takes place in the earliest stages of ribosome production.

"At this point in time, the RNA is not yet folded and compressed and is therefore accessible for modification by enzymes, which is not possible later in the mature and compact ribosome," explains Prof. Hurt. In this process, there is an interaction between biogenesis factor Cms1 and a specific area of the still immature RNA. "The central function of Cms1 is to prevent the bonding of other biogenesis factors until the RNA is chemically altered at specific sites," says Dr. Benjamin Lau, a research assistant on Prof. Hurt's team.

With their findings on the mechanisms leading to functional ribosomes, the researchers also hope to gain a better understanding of diseases such as ribosomopathies, which are based on defective maturation processes. According to Prof. Hurt, there are also clear indications that ribosomal RNA modifications could play a role in the development of cancer. Cancer cells depend on the accelerated production of ribosomes, explains the Heidelberg researcher.

More information: Benjamin Lau et al, Cms1 coordinates stepwise local 90S pre-ribosome assembly with timely snR83 release, *Cell Reports* (2022). DOI: 10.1016/j.celrep.2022.111684

Provided by Heidelberg University