Projet de Recherche PostDoctoral : Eukaryotic membrane proteins production in *E. coli*: a new look at inclusion bodies formation and rare codon cluster function

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Escherichia coli, the most widely used host in structural biology of membrane proteins (MPs), accounts for 200 of the 440 MP structures found in the PDB. Nevertheless this success is still limited to prokaryotic MPs; extending MP production in *E. coli* to eukaryotic sequences is then a real challenge. We want to address the formation of inclusion bodies of eukaryotic MP in *E. coli* following the idea that eukaryotic coding sequences are not adapted to the dynamic of the *E. coli* translation machinery. MP expression in *E. coli* is regulated at the translational level, inter alia, by rare codons repression. In yeast, a conserved set of Rare Codon Clusters (RCCs) is related to the secondary structure and intra-ribosomal folding of the protein. Therefore we will search for RCCs rules in the *E. coli* proteome and target proteins in order to design synthetic eukaryotic coding sequences adapted to the translation kinetics of *E. coli*. In addition to the classical *in vivo* approach, Cell Free Synthesis (CFS) will be further explored. As proof of concept we will focus on SQR (Sulphite quinone reductase) a monotopic MP involved in sulfide metabolism since it represents the paradigm of the intrinsic information possibly hidden in the RCCs.