

*Inside structure of the EFL1, SBDS and their complex*

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Ribosome biogenesis is closely linked to the cell growth and proliferation. Dysregulation of this process causes several diseases collectively known as ribosomopathies. For the final step of the maturation of the ribosome, the nascent 40S and 60S subunits are exported from the nucleus to the cell cytoplasm. To prevent premature association of these ribosomal subunits, eukaryotic initiation factor 6 (eIF6) binds the 60S subunit within the nucleus. Its release in the cytoplasm requires the interaction of EFL1 and SBDS proteins. In Shwachman-Diamond syndrome (SDS), a defective SBDS protein prevents eIF6 eviction, inhibiting its recycle to the nucleus and subsequent formation of the active 80S ribosome. We have shown that the interaction of EFL1 with SBDS resulted in a decrease of the Michaelis-Menten constant (KM) for GTP and thus SBDS acts as a GEF for EFL1 [1]. Subsequent studies demonstrated that SBDS debilitates the interaction of EFL1 with GDP without altering that for GTP [2]. The interaction of EFL1 alone or in complex with SBDS to guanine nucleotides is followed by a conformational rearrangement. Understanding the molecular strategy used by SBDS to disrupt the binding of EFL1 for GDP and the associated conformational changes will be key to understand their mode of action and alterations occurring in the disease. In this study, we aim to show, using BIO-SAXS and ab-initio modelling techniques, the conformational changes in EFL1 during its mutation [3] and the results from the interactions between EFL1 and its binding partners, the SBDS protein and the guanine nucleotides .

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