

Coordinated Regulation of Stem Cell Proliferation and Differentiation by Rna-Binding Proteins Cooperating with Ccr4-Not Deadenylase Complex in *C. Elegans*

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Uncovering molecular mechanisms regulating the balance of stem cell proliferation and differentiation can help us understand the causative factors for ageing, cancer and various degenerative disorders. Pumilio and FBF (PUF) family RNA-binding proteins are highly conserved regulators of stem cell development. We are investigating how PUF proteins regulate proliferation and differentiation of stem cells using *C. elegans* as a model organism. FBF-1 and FBF-2, two PUF family proteins in *C. elegans*, are required for maintaining germline stem cells by translational repression of their target mRNAs (Crittenden et al., 2002). FBF-1 and FBF-2 are very similar in primary sequence and share target mRNAs (Prasad et al., 2016, Kershner et al., 2010 and Porter et al., 2018), but we found that they have differential effects on target mRNAs and maintained stem cell numbers. Our findings suggest that FBF-1 may destabilize target mRNAs while FBF-2 may protect targets from degradation; FBF-1 may slow stem cell proliferation and differentiation whereas FBF-2 may promote stem cell proliferation and differentiation in coordinate fashion. Additionally, we found that FBF-1 activity in stem cells requires CCR4-NOT deadenylase machinery that shortens poly (A) tail of mRNA leading to mRNA instability. By contrast, FBF-2 activity in stem cells shows less dependence on CCR4-NOT, which is related to FBF-2 interaction with its specific cofactor, DLC-1. We propose that FBF-1, but not FBF-2, interacts with CCR4-NOT complex in stem cells. We are going to test this hypothesis by performing proximity ligation assay. In conclusion, our study uncovered mechanisms of PUF proteins controlling stem cell proliferation and differentiation through differential cooperation with CCR4-NOT deadenylase machinery.