DISSECTING THE CONTRIBUTION OF THE EIF3 SUBUNITS TO COMPONENT EVENTS DURING TRANSLATION INITIATION

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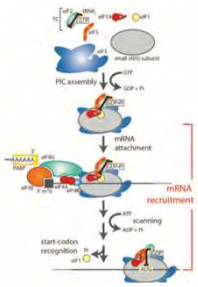
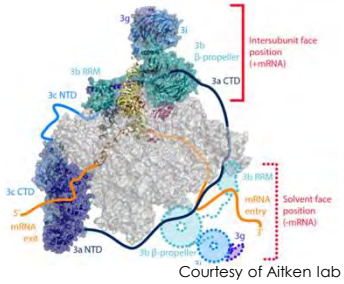
eIF3 is the largest pre-initiation factor in the pre-initiation complex

The pre-initiation complex (or "PIC" for short) is the name given to the ribosomal subunits and proteins that assemble and scan through mRNA prior to translation. One of these "parts" is eIF3, a complex of its own made up of 5 subunits that allow for it to play a role in translation initiation. Yet, as to what each of these subunits is individually responsible for is still not fully understood. By understanding the roles of the different subunits of eIF3, one can therefore better understand the eIF3 complex's role in translation initiation, which is why our goal is to disentangle the contributions of eIF3i and eIF3g from those of eIF3a, eIF3b, and eIF3c in order to approach doing just that.



Courtesy of Aitken lab

eIF3's presence in the pre-initiation complex



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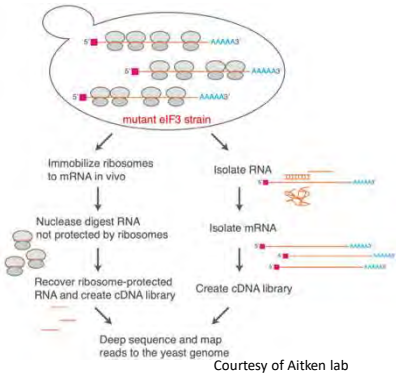
Ribosome profiling allows for the identification of mRNAs sensitive to initiation factor mutations

To investigate the role of eIF3 in translation initiation, we employ ribosome profiling, which enables us to learn the position of each translating ribosome on every mRNA in living cells. We use ribosome profiling to monitor the effects of specific mutations to the eIF3 complex and investigate the features of the specific mRNAs most sensitive to these mutations.



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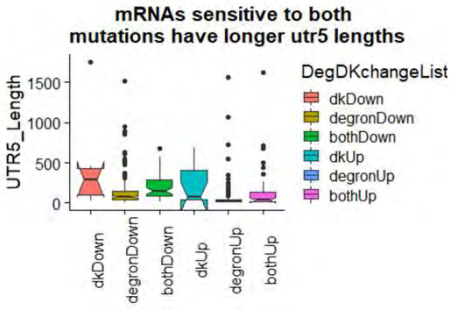
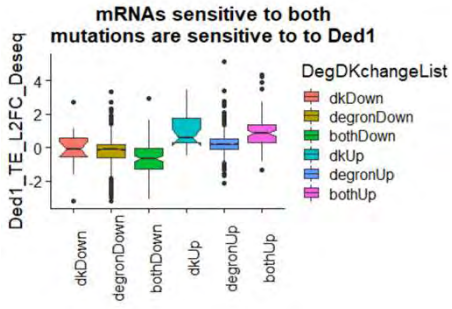
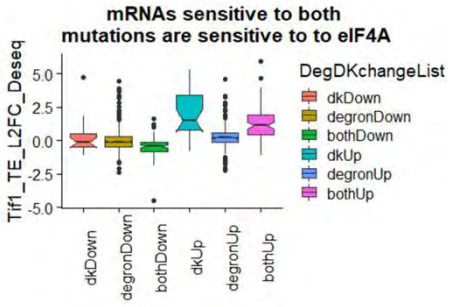
We are focusing on two mutations to eIF3: one disrupting the association of eIF3i and eIF3g with the rest of the eIF3 complex (*DDKK*) and another that disrupts the entire eIF3 complex (*Degron*). By comparing the mRNAs sensitive to both *DDKK* and *Degron* mutations to those mRNAs uniquely sensitive to the *Degron* mutation, we can reasonably find which contributions are made by eIF3i and g as opposed to being made by eIF3a,b, and c.

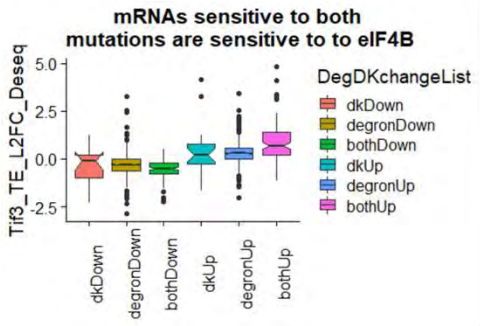
Evidence points to eIF3g and eIF3i being important for scanning

This analysis reveals that mRNAs that appear more sensitive to disruption of eIF3i and eIF3g have longer 5' UTR lengths and are more sensitive to mutations of the helicases Ded1 and eIF4A or to the initiation factor eIF4B. These observations are all apparent in the graphs below and are also consistent with a growing body of evidence that shows that subunits eIF3i and eIF3g play important roles in the scanning step of translation initiation.









eIF3i and eIF3g must still be investigated further, as well as the remaining subunits of the eif3 complex

Some questions that are of interest moving forward pertain to delving deeper into eIF3i and g to see what makes the two different from one another, if such a difference exists. We are also interested into why it is that these two subunits are more closely related to scanning then to a different process important to translation initiation. There is also the case of eIF3a,b, and c, which can be investigated similarly to how eif3i and g were in order to identify distinguishing features/ roles for all three.

A note on the pandemic's influence

Of course, it should be noted that at the time of this project's undertaking there were complications caused by a worldwide pandemic (Covid-19). However, such complications were likely not to have been detrimental to the results of this project since the data analyzed during this project had been collected prior to the onset of the pandemic.

Acknowledgments
URSI, Colin Echeverría Aitken