Poster

Nuclear organization in a Caenorhabditis elegans model for Nestor-Guillermo Progeria Syndrome

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ABSTRACT

Nestor-Guillermo progeria syndrome (NGPS) is a rare disease causing premature aging. This syndrome has features of classic progerias, although NGPS patients have no sign of cardiovascular impairments like in other progeroid syndromes. In contrast, they suffer profound skeletal abnormalities that affect their quality of life. A missense mutation in the BANF1 gene (c.34G > A [p.Ala12Thr]) causes NGPS in humans. BAF-1 is a member of the barriers-to-autointegration factor protein family and when mutated, results in a protein where the alanine 12 is replaced by a threonine residue causing a disruption in the nuclear envelope structure. Since baf-1 is a highly conserved protein present in all animals, we can use C. elegans as organism to model NGPS(In this nematode, it is a glycine mutated to a threonine residue in the same position). Understanding how the mutated BAF-1 protein works and how it interacts with other proteins from the nuclear envelope and with chromatin is essential to learn more about this syndrome and perhaps aging per se.

In order to generate a suitable NGPS model, cloning techniques were used to obtain the Crispr/Cas9 plasmids with the protein BAF-1 mutated (BAF-1 G12T), to later on be able to edit the nematode genome having the endogenous baf-1 locus mutated. Also DamID plasmids were generated in order to characterize the interaction profile between BAF-1 G12T and chromatin. Microinjection was performed to obtain the transgenic strains. Setting up crosses between our new strains and others with fluorescent markers, will allow us to obtain the attempted final strain that will carry BAF-1 G12T::Dam in chromosome II and baf-1 mutated in the endogenous locus.

Further studies are necessary, if our model is viable, in order to know more about how BAF-1 G12T behaves in C. elegans. To date, the baf-1 G12T::Dam transgenic strain has been generated and we are working on obtaining the other one.

REFERENCES

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