Group name: **Development and assembly of bilateral neural circuits**
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Title of the MRP/TFM:

Analysis of mRNAs locally translated in neuronal growth cones during axonal navigation.

Summary of the Project:

The intricate network of neural connections that form the adult brain is established during embryonic development. After differentiation into diverse neuronal types, these cells begin to extend their axons to connect with other neurons that are sometimes found on very distant places. Defects in axonal guidance during development occur mainly because axons are unable to respond to surrounding stimuli and fail to cross the midline correctly in pathologies including agenesis of the corpus callosum, horizontal gaze palsy with progressive scoliosis (HGPPS) or albinism.

Messenger RNA (mRNA) has been shown to be present in axons, and not just in somas of neurons as previously thought, suggesting that these axonal mRNAs could be locally translated "on demand" in the growth cones during axonal navigation in response to environmental stimuli. Actually, we know several cues and guidance molecules that are essential for axonal navigation during development to correctly connect neurons with each other. However, we do not currently know neither local translation is a mechanism implicated in the steering of the visual axons when they are approaching to the optic chiasm nor, in this case, which mRNAs are translated in the visual axons in response to different external stimuli to elicit repellent or attractive axonal behavior in mammals. This process of local protein synthesis, especially important in axonal guidance, would allow axons to respond to an attractive or repulsive stimulus immediately. The implications of understanding this mechanism are essentials because it provides a fast response capacity in different situations, not only during development but also against pathologies or axonal damage.

Using tools developed in our laboratory, we have identified mRNAs that are translated into retinal axons, both the ones that cross the midline (contralateral axons) and the ones that avoid the midline (ipsilateral axons). Now, we would like to validate them using firstly, molecular biology techniques to overexpress or remove genes and secondly, *in vivo* imaging performing fluorescence recovery after photobleaching to demonstrate the local translation of different molecules to understand the mechanisms that regulate axonal guidance and neuronal connectivity. The results obtained from this proposal will allow us to delve into the mechanisms and molecules involved in axonal guidance helping us to identified molecules with a possible role in regeneration to mitigate and/or prevent their associated pathologies.

Methods and technology involved in the MRP/TFM Project:

PCR, cloning, IHC, ISH, confocal microscopy, fluorescence recovery after photobleaching, image processing.

Member/s of the lab who will act as tutor/co-tutor of the project (if different from the group IP):

Dr. Verónica Murcia.

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