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AR-NMJ - Decoding molecular sexual dimorphism of neuromuscular function

Our ability to move, whether it is running, breathing, or even small everyday actions, depends on electrical signals that trigger muscles to contract at the connection point between nerves and muscles, called the neuromuscular junction (NMJ). Differences between sexes, such as hormone levels and genetics, affect how these junctions respond and how they may break down in disease, but the exact mechanisms and molecules involved are still unclear. This project aims to unravel how sex hormones influence and preserve NMJs by exploring how hormone receptors outside the cell nucleus work. Indeed, the androgen receptor (AR) is found in the nucleus where it exerts its transcription activity, but also at the edges of neurons. When the AR gene is mutated, it leads to spinal and bulbar muscular atrophy (SBMA), a neuromuscular disease characterized by motor neuron loss and muscle wasting. Because preliminary data shows that AR interacts with both the protein-making machinery and RNA-binding proteins, the ERC-funded AR-NMJ project will explore whether AR is part of this protein production machinery at the neuronal periphery and whether AR outside the nucleus helps maintain the stability of neuromuscular junctions (NMJs) through hormone binding, mechanisms that can contribute to SBMA. This will shed light not only on a novel disease mechanism in SBMA, but also on possible neglected functions of other hormone receptors, such as estrogen, progesterone and other steroid receptors.

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