Short Communication

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Synuclein in Prrx1-positive cells causes partial loss of function in the central nervous system

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Abstract

α-Synuclein is a small 140 amino acid polypeptide encoded by the *Snca* gene that is highly expressed in neural tissue, but it is also found in osteoblasts, erythroblasts, macrophages, and adipose tissue. Previously, using co-expression network analysis we found that *Snca* was a key regulator of skeletal homeostasis, and its deletion partially prevented bone loss after ovariectomy (OVX). Here we tested the hypothesis that *Snca* deletion in mesenchymal progenitors using the Prrx1Cre (Prrx1, Paired-related homeobox 1) limb enhancer would protect bone mass after OVX. Prrx1Cre;Snca$^{fl/fl}$ and littermate controls (Snca$^{fl/fl}$) were sham operated or ovariectomized (OVX) at 8 weeks of age and sacrificed at 20 weeks. Independently, eight-week female and male Prrx1Cre;Snca$^{fl/fl}$ mice and littermate controls were administered a high fat (60% fat) or low fat (10% fat) diet for 15 weeks. Bone loss was not prevented in either genotype after ovariectomy, but the Prrx1Cre;Snca$^{fl/fl.}$ mice were partially protected from weight gain after OVX and high fat diet (HFD). Serum catecholamine levels were lower in the Prrx1Cre;Snca$^{fl/fl}$ both on a low fat diet (LFD) and HFD versus fl/fl controls. Importantly, mutant mice exhibited a number of physical and behavioral phenotypes that were associated with conditional deletion of *Snca* in several brain regions. Cells labeled with Prrx1 were noted throughout the central nervous system (CNS). These data support earlier preliminary reports **of** Prrx1 expression in neural progenitors, and raise a cautionary note about the evaluation of skeletal and body composition phenotypes when using this Cre driver to study osteoprogenitor development.

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Biography

I'm a researcher and designer convinced that working with living systems amounts to a potential transfiguration of contemporary concepts of design. My work combines material explorations and interventions to interrogate the possibilities at the intersection of living systems and design, and aims to develop non-deterministic approaches that engage with the non-human on an equal footing.

I'm currently working on a project that looks at fighting antimicrobial resistance by integrating beneficial microbes into buildings to encourage health benefits..