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LONG-TERM EFFICACY OF CELL THERAPY IN A NONHUMAN PRIMATE MODEL OF STABLE URINARY SPHINCTER DEFICIENCY.

Hypothesis / aims of study
The goal of this study was to measure the long-term efficacy of muscle precursor cell therapy in a nonhuman primate (NHP) model of urinary sphincter deficiency. It is hypothesized that local injection of autologous skeletal muscle precursor cells (skMPCs) provides long-term (the equivalent of a three year follow-up) restoration of both sphincter structure and function in this animal model that sits at the nexus of clinical translation.

Study design, materials and methods
Urinary sphincter deficiency was created in adult female cynomolgus monkeys by selectively cauterizing and then transecting the pudendal innervation of the sphincter complex. Monkeys received (n=18), or did not receive (n=18) intra-sphincter injections of 5 million autologous green fluorescence protein (GFP) -labeled skeletal muscle precursor cells. Four uninjured, no treatment monkeys were used as Controls. Maximal urethral pressures and corresponding histological analysis of the structural and cellular components of the sphincter complex were measured at defined time-periods - up to 12 months post-injection.

Results
Pudendal denervation reduced ($p<0.05$) and cell therapy produced sustained increases maximal urethral pressures to within baseline values ($p>0.05$) and restored sphincter muscle/collagen content to within control values ($p>0.05$). GFP^+ cells were found in close proximity with, or incorporating into, restored skeletal muscle bundles, somatic and adrenergic innervation and the vasculature, but only in small numbers. Both native and injected cells readily expressed the chemokine CXCL-12. In a concurrent preliminary study, sphincter injection of CXCL-12 (n=3) produced similar functional and structural improvements as the cell therapy.

Interpretation of results
Cell injections resulted in long-term structural and functional regeneration in the injured sphincter complex in this model. The role of skMPCs in regeneration appears to involve active incorporation into regenerating sphincter complex.

Concluding message
We speculate they may also stimulate migration of native cells to the sphincter complex through chemokine mechanisms.

Disclosures
Funding: National Institutes of Health, NIDDK **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Female Cynomolgus monkeys (Macaca fascicularis) **Ethics Committee:** Institutional Animal Care and Use Committee