Development of Myogenic IAS Reconstructs from Human Internal Anal Sphincter (IAS) Smooth Muscle Cells (SMCs) with Functional and Molecular Properties Similar to Intact Human IAS

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Development of Myogenic IAS Reconstructs from Human Internal Anal Sphincter (IAS) Smooth Muscle Cells (SMCs) with Functional and Molecular Properties Similar to Intact Human IAS
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Backgrounds & Aims
Rectal incontinence is associated with defective Internal Anal Sphincter (IAS). Current therapies are not satisfactory, raising a potential for the replacement of the dysfunctional IAS with the reconstructs. Present studies were performed to develop human IAS smooth muscle reconstructs with functional and molecular attributes similar to the intact human IAS smooth muscle (SM).

Methods
SMCs were isolated from Human IAS tissue samples, and cultured in collagen coated tissue culture dishes with DMEM containing 10% fetal bovine serum and 50 mg/ml of sodium ascorbate, around the central Syngard posts. Method for preparation of Syngard posts was modified from Hecker et al., Am J Physiol 2005. Collagen I-based IAS reconstructs were made and their physiological properties were compared with intact human IAS.

Results

Methods

Fig. 1. A typical tracing of the characteristic responses of above developed IAS reconstructs from human IAS-SMCs. PKC inhibitor G-6850 causes minimal decrease in the basal tone, while ROCK inhibitor Y27632 almost completely abolishes the tone, close to 0.

Summary & Conclusions
- The studies for first time show that presently prepared IAS reconstructs from human IAS SMCs are functionally and molecularly similar to intact human IAS.
- Data further show that basal tone in these IAS reconstructs is primarily dependent on Rho/ROCK pathway.