

Exploring the fertility rescue effect of transgenic expression of human PRSS55 in *Prss55* null mice

Courtney M. Sutton^{1,2}, Alexis R. Souto^{1,2}, Thomas X. Garcia^{1,2,3}, and Martin M. Matzuk^{1,2,*}

¹Center for Drug Discovery, Baylor College of Medicine, Houston, TX; ²Department of Pathology & Immunology, Baylor College of Medicine, Houston, TX; ³Scott Department of Urology, Baylor College of Medicine, Houston, TX

The need for a non-hormonal male contraceptive pill for men still exists. Serine protease 55 (PRSS55) is a male reproductive tract-specific protein that when knocked out in mice leads to male infertility, making it a viable contraceptive target. The goals of our studies were to determine whether we could rescue fertility in *Prss55* KO mice with human PRSS55, allowing for a more suitable animal model to test the efficacy of drug candidates. We used pronuclear injection to generate transgenic mice expressing tagged-human PRSS55 protein. We then crossed the transgenic mice with *Prss55* KO mice to generate a rescue line. After generating our mouse lines, we then performed a fertility assessment, analyzed testes and epididymis grossly and histologically, and determined sperm parameters of each line. Morphological differences were observed between our rescue mouse lines and our WT mice when comparing body weight and testis weight, where humanized transgenic mice had lighter weights. Apart from hyperactivation, where rescue males had decreased hyperactivation, all other sperm parameters were similar between the two groups. Our humanized transgenic mouse lines' poor ability to rescue fertility might be accounted for because of the low homology (57%) between human and mouse PRSS55. PRSS55 is required for male fertility and is a viable target as a small molecule for non-hormonal male contraceptive.

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