Aromatase Expression in Uterine Leiomyomata is Regulated by Alternative Promoters

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Objective: The objective is to determine the alternatively used promoters responsible for aromatase expression in uterine leiomyomata. Steroid hormones are essential for the progression of leiomyomata. Aberrant expression of aromatase, the key enzyme in estrogen biosynthesis, has been detected in leiomyoma tissue but not in disease-free myometrium. The gene that encodes aromatase contains 10 tissue-specific promoters. The aim of this study is to elucidate the promoters responsible for aromatase expression in leiomyoma tissue.

Methods: We isolated total RNA samples from leiomyoma (n=24) and adjacent myometrium (n=6) samples as well as myometrium from disease-free uteri (n=1) from 23 patients. They were African-American, hispanic or white. We amplified the unknown 5'-UT ends of aromatase mRNA by 5'-RACE and then we cloned, sequenced and mapped them to the human genome.

Results: We cloned aromatase mRNA in 14 out of 24 (58 %) leiomyoma samples. A total of 21 promoters are cloned in 14 leiomyoma samples. The distribution of promoter-specific aromatase mRNA species was as follows: nine promoter I.3 (64 %), four promoter I.6 (28.5%), three promoter 2.a (21.4 %), three promoter II (21.4 %), two promoter I.4-specific mRNA (14.3 %). One myometrial sample adjacent to leiomyoma contained promoter I.3-specific aromatase mRNA (17 %). No amplification was observed in myometrium from disease-free uteri.

Conclusion: The primary promoter region responsible for aromatase expression in uterine leiomyomata seems to be promoter I.3/II. In contrast to reports on tissues from Japanese patients, we found limited use of promoter I.4, which is different than promoter I.3 in terms of regulation, tissue-specificity and sequence. This may be due racial differences.Verification of these preliminary results in a larger population is under way. Supported by the NIH award HD46260.