

Repurposing Tranilast to Treat Uterine Fibroids

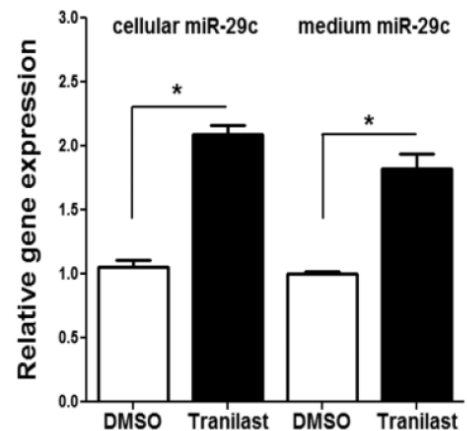
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Background

- Uterine fibroids (leiomyomas) are the most common benign pelvic tumors and develop in ~80% of women during their reproductive years.
- Symptoms include pelvic pain, abnormal uterine bleeding, pelvic pressure, and infertility.
- Initial treatments focus on alleviating symptoms and include the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and iron supplements.
- Surgery is often used to treat leiomyomas, posing a financial burden of almost \$2.2 billion a year on the U.S. healthcare system. Surgery, however, is expensive and some insurance plans do not cover the surgical removal of fibroids. In addition, fibroid surgeries can lead to complications for future pregnancies and/or the inability to have children.
- Several hormonal therapies have been used as alternative interventions for growth inhibition and symptom management but are not suitable for long-term use due to their side effects.
- In summary, surgical procedures are costly and may result in health complications, while hormonal therapies are only a short-term solution.
- A non-hormonal, non-surgical treatment is urgently needed to treat the millions of women suffering from uterine fibroids.

Innovation

- Dr. Khorram has discovered that two miRNA families – miR-29 and miR-200 – play critical roles in fibroid pathogenesis.
- For example, the expression of miR-29c and miR-200c are significantly reduced in leiomyomas and are inversely correlated with the expression of several genes that regulate extracellular matrix (ECM) composition and the cell cycle.
- In addition, Dr. Khorram has found that **Tranilast**, an anti-allergic drug approved in Asia, restores the expression of microRNAs in the miR-29 and miR-200 families, which results in tumor shrinkage, a reduction in inflammation, and a decreased accumulation of ECM and fibrosis.
- Stage of development:
 - *In vitro* experiments have been completed in leiomyoma smooth muscle cells isolated from patient samples.
 - Two-month treatment with Tranilast in a mouse xenograft model of human fibroids resulted in a significantly diminished fibroid size.
- Future milestones: Dr. Khorram plans to develop novel, more potent variants of Tranilast and test them for safety and clinical efficacy in his fibroid mouse model, then move to human studies.



Bar graph shows increased miR-29c levels in both leiomyoma cells and conditioned medium after treatment with Tranilast compared to DMSO alone.

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Advantages

- Non-surgical and non-invasive
- Orally administered synthetic drug
- No hormonal side effects
- Approved as an anti-allergic in Asia

Applications

- Treatment of uterine leiomyomas
- Treatment of other fibrotic disorders

About the inventor

- Omid Khorram, MD, PhD, is a Lundquist Institute investigator and the Chief of the Division of Reproductive Endocrinology and Infertility at the Harbor-UCLA Medical Center.
- Dr. Khorram is a practicing obstetrician and gynecologist with over 30 years of experience.
- Dr. Khorram is an active research investigator – he has published over 80 peer-review manuscripts and has been supported by NIH funding.

Research Focus

- The focus of Dr. Khorram's laboratory is to determine the mechanisms underlying the pathogenesis of uterine fibroids.
- Dr. Khorram and his team aim to discover novel, **non-hormonal** therapies for fibroids.
- They are seeking partnerships with companies interested in Women's Health, either through working together to submit SBIR grants or through sponsored research and licensing.

IP Status

- U.S. Patent 10,517,842 titled "Methods of modulating miRNA levels and compositions for use in the same" issued 12/31/2019.