

Developing Small Molecules for Uterine Fibroid Treatment

[LAB0229]

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 fibroid tumors have aberrant metabolism and certain metabolic enzymes are significantly overexpressed.
- His research shows that there is a racial dependence in the overexpression of these enzymes, which aligns with the known racial disparity in fibroid prevalence and degree of symptom severity.
- Dr. Khorram and his team have found inhibitors that target the overexpressed metabolic enzymes and are promising candidates to shrink fibroid tumors in patients.
- Stage of development:
 - *In vitro* experiments using the inhibitors to treat leiomyoma smooth muscle cells isolated from patient samples show a reduction in cell growth.
 - In a mouse fibroid xenograft model, tumors treated with the inhibitors significantly decrease in size.
- Future milestones: Further funding is needed to develop more potent inhibitors of the identified enzymes. Dr. Khorram plans to:
 - Complete a screen for additional inhibitors to the identified enzymes
 - Create more potent variants of the inhibitors
 - Complete pre-clinical testing and delineate a mechanism of action and a better understanding of how these inhibitors reduce fibroid size

Advantages

- Non-surgical and non-invasive
- No hormonal side effects

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Applications

- Treatment of uterine leiomyomas

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 Application No. 17/365,723 filed July 1, 2021 – pending

Publications

- Chuang TD, Quintanilla D, Boos D, Khorram O. Tryptophan catabolism is dysregulated in leiomyomas. Fertil Steril. 2021 Oct;116(4):1160-1171. doi: 10.1016/j.fertnstert.2021.05.081. Epub 2021 Jun 9. PMID: 34116832.