Inhibitors Of The N-Terminal Domain Of The Androgen Receptor

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OTHER INFORMATION

KEYWORDS

Therapeutics & Vaccines, oncology

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - New Chemical Entities, Drug Leads
  - Therapeutics

RELATED CASES

2017-094-0

SUMMARY

UCLA researchers under the guidance of Drs. Matthew Rettig and Mike Jung have developed a novel family of therapeutics for use against castration resistant prostate cancer. These drugs have been shown to inhibit the androgen receptor and are unaffected by the most common drug-resistant mutations found in prostate cancer patients.

BACKGROUND

Prostate cancer is the most commonly diagnosed cancer and the second leading cause of cancer death in Western men. When the cancer is confined locally, the tumor can be eradicated by surgery or radiation. However, 30% of such tumors will eventually relapse with distant metastatic disease, and other patients have advanced disease at diagnosis. Metastatic disease is treated by chemical castration and/or androgen deprivation therapy. This treatment is intended to lower the circulating levels of androgens, effectively reducing the activation of the androgen receptor.

Although initially effective, these treatments quickly fail as the cancer becomes hormone-refractory, resulting in castration resistant prostate cancer (CRPC). Following the failure of androgen deprivation therapy, patients can be treated by directly targeting the androgen receptor (AR), as with AR antagonist enzalutamide. However, most patient tumors will eventually develop resistance, typically by expressing a constitutively-active AR resulting from a mutation or splice variant that truncates the C-terminal domain.

INNOVATION

Dr. Matthew Rettig, Medical Director of the Prostate Cancer Program of the Institute of Urologic Oncology, and Dr. Michael Jung from the Department of Chemistry & Biochemistry have synthesized novel inhibitors targeting the N-terminal domain of the androgen receptor. These compounds have anticancer activity in castration resistant prostate cancer (CRPC) cell lines, showing improved activity compared to current CRPC therapeutics. The lead compound also inhibits prostate cancer cell lines containing the most common splice variants found in CRPC, specifically AR-V7 and AR-V567.

APPLICATIONS

- Use as therapeutic treatment for castration resistant prostate cancer
- Use as therapeutic treatment for drug-resistant castration resistant prostate cancer

ADVANTAGES

- Inhibits wild-type and splice variant androgen receptor
- Does not inhibit transcriptional activity of glucocorticoid receptor
- Inhibits growth *in vitro* in dose-dependent fashion
- Better inhibition compared to current approved therapies in reporter assay

STATE OF DEVELOPMENT

in vitro cellular assay

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	12,162,818	12/10/2024	2017-094
Germany	Issued Patent	602018066215.4	03/06/2024	2017-094
European Patent Office	Issued Patent	3571183	03/06/2024	2017-094
France	Issued Patent	3571183	03/06/2024	2017-094
United Kingdom	Issued Patent	3571183	03/06/2024	2017-094
Japan	Issued Patent	7443414	02/26/2024	2017-094
China	Issued Patent	201880012231.0	06/30/2023	2017-094
United States Of America	Issued Patent	11,261,152	03/01/2022	2017-094
European Patent Office	Published Application	4397652	07/10/2024	2017-094

Additional Patents Pending

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