Compounds that Interfere with the Androgen Receptor Complex

Summary (1024-character limit)
NCI researchers have identified novel compounds that inhibit FKBP52-mediated activation of the androgen receptor protein (AR), a major target for anti-prostate cancer therapeutic development. As FKBP52 is implicated in the regulation of other hormone receptors, anti-FKBP52 may be applicable in the treatment of hormone-dependent diseases such as diabetes or even used as contraceptives. NCI seeks partners to license or co-develop this technology.

NIH Reference Number
E-162-2009

Product Type
- Therapeutics

Keywords
- androgen receptor protein, prostate cancer, diabetes

Collaboration Opportunity
This invention is available for licensing and co-development.

Contact
- John D. Hewes
  NCI - National Cancer Institute

  240-276-5515

  John.Hewes@nih.gov

Description of Technology

Investigators at the National Institutes of Health (NIH) have discovered compounds that have potential as novel anti-androgen therapeutics. The immunophilin protein FKBP52 is part of a protein complex that helps fold the androgen receptor (AR) protein, a target for treating prostate cancer, and enhances its activity. Disruption of the FKPB52-AR interaction greatly reduces the activity of the AR. With the goal of finding potential therapeutic compounds that inhibit the FKBP52-mediated activation of AR, several small molecules were tested and found to be antagonists of FKBP52 and to inhibit AR activity in prostate cells. These compounds can serve as therapeutics for the treatment of prostate cancer and benign prostate enlargement. Moreover, FKBP52 is also implicated in the regulation of other hormone receptors so these compounds could be used to treat other hormone-dependent diseases such as diabetes or even used as contraceptives.

One of the standard treatments for prostate cancer makes use of anti-androgens, like bicalutamide, which compete for binding with the natural male hormones to AR and inhibit their proliferative activity. The problem with available anti-androgen drugs is that prostate tumors eventually become drug resistant resulting in so-called androgen-resistant prostate cancer. One cause of this is an increase in the levels of AR produced by the prostate cancer cells. A solution to this problem may lie in disrupting the protein folding of AR by interfering with its interaction with FKBP52 using these compounds.

The Center for Cancer Research, Urologic Oncology Branch, seeks parties to co-develop, or license antagonists of FKBP52-dependent remodeling of the androgen receptor.

Potential Commercial Applications

- Use of the compounds for treatment of prostate cancer and benign prostate enlargement
- Use of the compounds in treating insulin-independent diabetes
- Use of the compounds as male or female contraceptives
- Use in screening for compounds that inhibit of FKBP52-enhanced AR activity

Competitive Advantages

- The compounds do not compete with androgens and specifically inhibit FKBP52-enhanced AR function
- Potential for synergistic use with conventional anti-androgens for treatment of androgen resistant prostate cancer

Inventor(s)

Leonard Neckers (NCI), Marc Cox

Development Stage

- Pre-clinical (in vivo)

Publications

De Leon JT et al [Proceedings of the National Academy of Sciences 108(29), 11878-83 (2011)]

Cheung-Flynn et al. [15831525]

Patent Status

- **U.S. Patent Issued:** U.S. Patent Number 8859207, Issued 14 Oct 2014
- **U.S. Patent Issued:** U.S. Patent Number 9233973, Issued 12 Jan 2016
- **Foreign Filed:** Foreign Filed - Patent Application 61/242,541

Related Technologies

- E-065-2013

Therapeutic Area

- Hormonal Systems, Endocrine, and Metabolic Diseases