May 20th, 12:30 PM

ErbB2 Signaling Increases Androgen Receptor Expression in Abiraterone-Resistant Prostate Cancer

Shuai Gao  
University of Massachusetts Boston

Huihui Ye  
Beth Israel Deaconess Medical Center

Sean Gerrin  
Beth Israel Deaconess Medical Center

See next page for additional authors

Follow this and additional works at: https://escholarship.umassmed.edu/cts_retreat

Part of the Cancer Biology Commons

Gao, Shuai; Ye, Huihui; Gerrin, Sean; Wang, Hongyun; Sharma, Ankur; Chen, Sen; Patnaik, Akash; Sowalsky, Adam; Voznesensky, Olga; Han, Wanting; Yu, Ziyang; Mostaghel, Elahe; Nelson, Peter S.; Taplin, Mary-Ellen; Balk, Steven P.; and Cai, Changmeng, "ErbB2 Signaling Increases Androgen Receptor Expression in Abiraterone-Resistant Prostate Cancer" (2016). UMass Center for Clinical and Translational Science Research Retreat. 23.
https://escholarship.umassmed.edu/cts_retreat/2016/posters/23

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.
**Presenter Information**
Shuai Gao, Huihui Ye, Sean Gerrin, Hongyun Wang, Ankur Sharma, Sen Chen, Akash Patnaik, Adam Sowalsky, Olga Voznesensky, Wanting Han, Ziyang Yu, Elahe Mostaghel, Peter S. Nelson, Mary-Ellen Taplin, Steven P. Balk, and Changmeng Cai

**Keywords**
prostate cancer, ErbB2 signaling

**Creative Commons License**
This work is licensed under a Creative Commons Attribution-Noncommercial-Share Alike 3.0 License.
ErbB2 Signaling Increases Androgen Receptor Expression in Abiraterone-Resistant Prostate Cancer

Shuai Gao1, Huihui Ye2, Sean Gerrin3, Hongyun Wang4, Ankur Sharma5, Sen Chen6, Akash Patnaik7, Adam G. Sowalsky8, Olga Voznesensky6, Wanting Han1, Ziyang Yu3, Elahe Mostaghel9, Peter S. Nelson10, Mary-Ellen Taplin11, Steven P. Balk12, and Changmeng Cai1

1Center for Personalized Cancer Therapy, University of Massachusetts Boston
2Pathology, Beth Israel Deaconess Medical Center
3Hematology-Oncology Division, Beth Israel Deaconess Medical Center
4Medicine, BIDMC
5Department of Cancer Biology, Thomas Jefferson University
6Medicine, Beth Israel Deaconess Medical Center
7Medicine-Hematology/Oncology, University of Chicago
8Laboratory of Genitourinary Cancer Pathogenesis, National Cancer Institute
9Human Biology and Clinical Research, Fred Hutchinson Cancer Research Center
10Division of Human Biology, Fred Hutchinson Cancer Research Center
11Dana-Farber Cancer Institute
12Division of Hematology and Oncology, Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School

Abstract
Purpose: ErbB2 signaling appears to be increased and may enhance AR activity in a subset of CRPC, but agents targeting ErbB2 have not been effective. This study was undertaken to assess ErbB2 activity in abiraterone-resistant prostate cancer (PCa), and determine whether it may contribute to androgen receptor (AR) signaling in these tumors. Experimental Design: AR activity and ErbB2 signaling were examined in the radical prostatectomy specimens from a neoadjuvant clinical trial of leuprolide plus abiraterone, and in the specimens from abiraterone-resistant CRPC xenograft models. The effect of ErbB2 signaling on AR activity was determined in two CRPC cell lines. Moreover, the effect of combination treatment with abiraterone and an ErbB2 inhibitor was assessed in a CRPC xenograft model. Results: We found that ErbB2 signaling was elevated in residual tumor following abiraterone treatment in a subset of patients, and was associated with higher nuclear AR expression. In xenograft models, we similarly demonstrated that ErbB2 signaling was increased and associated with AR reactivation in abiraterone-resistant tumors, while ERBB2 message level was not changed. Mechanistically, we show that ErbB2 signaling and subsequent activation of the PI3K/AKT signaling stabilizes AR protein. Inhibitors targeting ErbB2/PI3K/AKT pathway disrupt AR transcriptional activity. Furthermore, concomitantly treating CRPC xenograft with abiraterone and an ErbB2 inhibitor, lapatinib, blocked AR reactivation and suppressed tumor progression. Conclusions: ErbB2 signaling is elevated in a subset of abiraterone-resistant prostate cancer patients and stabilizes AR protein. Combination therapy with abiraterone and ErbB2 antagonists may be effective for treating the subset of CRPC with elevated ErbB2 activity.

Contact information:
Shuai Gao, PhD  Shuai.gao@umb.edu  617-287-3447 UMass Boston