

**97th AACR Annual Meeting****April 1-5, 2006****Washington, DC** [Print this Page for Your Records](#)[Close Window](#)**Abstract Number:** 2178**Presentation Title:** PSA-activated proaerolysin as a prostate specific cancer therapy**Presentation Start/End Time:** Monday, Apr 03, 2006, 8:00 AM -12:00 PM**Location:** Exhibit Hall, Washington Convention Center**Poster Section:** 17**Poster Board Number:** 19**Author Block:** *Jeff L. Browning, Ralph Abi-Habib, Ravibhushan Singh, Carol Carter, Janelle Ortiz, Rosemina Merchant, J. Thomas Buckley, Samuel R. Denmeade, Arthur E. Frankel.*  
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Native proaerolysin is a channel-forming bacterial protoxin that is activated upon cleavage by host proteases such as furin. PRX302 is an engineered form of proaerolysin in which the furin cleavage site has been replaced with a sequence known to be preferred by the protease, prostate specific antigen (PSA). The goal of this study was to examine the suitability of PRX302 for use as a therapeutic agent in prostate cancer and benign prostatic hyperplasia as assessed by comparing proteolytic activation of PRX302 and native proaerolysin and their cytotoxicity towards PSA-producing and non-producing cell lines.

Modification of native proaerolysin to PRX302 markedly altered the activity of each of the proteases (chymotrypsin, trypsin, furin, and thrombin) tested toward this protein. Activity toward proaerolysin was decreased 10-100 fold for each of the proteases tested except PSA, which showed a 4-fold increase in activity against the modified protein. Of all enzymes tested, only PSA cleaved more PRX302 than proaerolysin. Indeed the ratio of PRX302 to proaerolysin cleavage by PSA was more than 40 times that of any other protease tested.

As expected, native proaerolysin was effectively cytotoxic at low pM concentrations in all cells tested (LNCaP, DU145, CWR22Rvi, PC3, PrEC, and RWPE2-W99). However, PRX302 was cytotoxic at low pM concentration only in normal (PrEC) and papilloma- transfected (RWPE2-W99) prostate cells, both of which produce active PSA.

In conclusion, PRX302 appears to be preferentially activated by PSA and selectively kills PSA producing cells. PRX302 deserves further study for possible treatment of prostate cancer and benign prostatic hyperplasia.

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