FEATURES

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Inhibiting Prostate Cancer Progression

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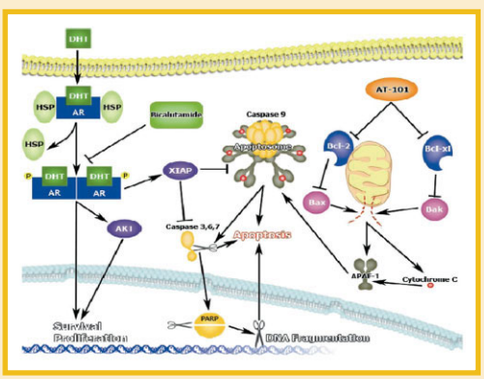
Prostate cancer remains a leading cause of cancer death in American men. Androgen deprivation therapy (ADT) is the most common treatment for advanced prostate cancer patients; however, ADT fails in nearly all cases resulting in castration resistant or androgen insensitive (AI) disease. In many cases, this progression results from dysregulation of the pro-survival Bcl-2 family proteins. Inhibition of pro-survival Bcl-2 family proteins, therefore, may be an effective strategy to delay the onset of AI disease. Gossypol, a small molecule inhibitor of pro-survival Bcl-2 family proteins, has been demonstrated to inhibit AI prostate cancer growth. This study by McGregor et al was undertaken to better understand the *in vitro* effects of androgen receptor (AR) on AT-101 induced apoptosis. Upon AR activation in combination with AT-101 treatment, apoptosis is reduced, cell survival increases, and caspase activation is attenuated. Akt and X inhibitors of apoptosis (XIAP) are downregulated in the presence of AT-101, and AR stimulation rescues protein expression. Combination treatment of bicalutamide and AT-101 increases apoptosis by reducing the expression of these prosurvival proteins. These data suggest that combination therapy of AT-101 and androgen deprivation therapy may further delay the onset of androgen insensitive disease, resulting in prolonged progression free survival of prostate cancer patients.



Adiponectin and Hepatic Fibrosis

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Recently adipocytokines, primarily produced by white adipose tissue (WAT), have been implicated as molecular mediators of liver fibrogenesis. The biological basis for the molecular interplay of leptin and adiponectin in the regulation of matrix production is timely as non-alcoholic fatty liver disease has become so widespread. In this article Handy, et. al. extend recent findings that adiponectin is protective against hepatic fibrosis. In this report they demonstrate that adiponectin upregulates matrix metalloproteinase I while conversely inhibiting available TIMP-1 protein availability in cultured hepatic stellate cells. More compelling are *in vivo* data revealing that adiponectin knockout mice are more vulnerable to develop liver fibrosis in the setting of leptin and carbon tetrachloride co-administration, and liver tissue expression of the Suppressors of Cytokine Signaling 3 (SOCS3) mRNA protein in these mice are markedly suppressed. Handy and colleagues demonstrate that adiponectin down-regulates leptin-mediated phosphorylation of Stat3 proteins—a downstream effector in the leptin signaling cascade which may be the result of activation of adenosine monophosphate kinase (AMPK)-related stabilization of SOCS-3 protein expression and a bi-phasic increase in SOCS-3mRNA. Their findings suggest adiponectin has hierarchical control of upstream leptin-signaling events, since both *in vivo* and *in vitro* adiponectin overrides the pro-fibrotic effects of leptin.