

FABP5-Related Signaling Pathway Used as Therapeutic Target for Castration-Resistance Prostate Cancer

Youqiang Ke

University of Liverpool, UK

Castration resistant-prostate cancer is largely impervious to feather hormonal therapy and hence the outlook for patients is grim. Here we use an approach to attach the recently discovered Achilles heel. The experimental treatments established in this study are based on the recent report that it is the FABP5-PPAR γ -VEGF signalling axis, rather than the androgen receptor activated pathway, played a dominant role in promoting the malignant progression of castration resistant prostate cancer cells. Treatments have been established in nude mice by suppressing the biological activity of FABP5 using a chemical inhibitor SBFI26 and a novel bio-inhibitor, dmrFABP5. Both inhibitors significantly suppressed the proliferation, migration, invasiveness and colony formation of PC3-M cells *in vitro*. They also produced a highly significant suppression of both metastatic rates and average sizes of primary tumours developed from cancer cells implanted orthotopically into the prostate gland of the mouse. Strikingly, the bio-inhibitor dmrFABP5, amutated FABP5 incapable of binding to fatty acids, produced a much better suppression of both primary tumour and metastasis. Both inhibitors interfere with the FABP5-PPAR γ -signalling pathway. SBFI26 can competitively bind to FABP5 and hence suppresses cellular fatty acid uptake. In contrast, dmrFABP5 can block the fatty-acid stimulation of PPAR γ and prevent it activating the down-stream regulated cancer- promoting genes. This is an entirely novel experimental approach to treating castration-resistant prostate cancer and is completely different from current treatments that are based on androgen-blockade therapy.

Biography:

Dr. Youqiang Ke finished his PhD in Leeds University and joined the Cancer & Polio Research Laboratories in Liverpool University in 1989 to work as a Postdoctoral Research Associate. In 1994, Dr. Ke got a lecturer position in the Department of Pathology in the same university and started his research work on the molecular mechanisms involved in the malignant progression of prostate cancer cells. Dr. Ke was promoted to a Senior Lecturer in 2001, a Reader in 2003 and a Full Professor in 2005. Dr. Ke is the Director of Molecular Pathology in the School of Cancer Studies, Liverpool University, United Kingdom.