USP26 gene is a regulation of androgen receptor signaling

The androgen receptor is a member of the nuclear receptor superfamily and is essential for male sexual differentiation and maturation, maintenance of spermatogenesis, prostate development, and normal prostate function.

Deregulation of this signaling pathway is highly associated with prostate cancer development and progression.

The prostate cancer is characterized by the transition from a hormone-dependent state to a hormone-independent state. The hormone-independent state might develop mutations of androgen receptor or this signaling axis might be tilted by changes of cofactor levels or activities (HDAC1, RNF6, K6/K27, CHIP, Hsp70/Hsp90, and TRIM68 ubiquitin ligase, PIRH2 and E6-AP).

Dirac AMG and Bernard R. suggest that USP26 gene with androgen receptor and other cofactors thereby contributing to regulation of androgen transcriptional activity.

Taken from:

Dirac AMG, Bernards R. The deubiquitinating enzyme USP26 is a regulator of androgen receptro signaling. *Mol Cancer Res.* 2010;8(6):844-54.

A phase I study of foretinib, a multi-targeted inhibitor of c-Met and vascular endothelial growth factor receptor 2

All patients received foretinib orally for 5 consecutive days every 14 days. Dose escalation followed a conventional "3+3" design. Responses were observed in two patients with papillary renal cell cancer and one patient with medullary thyroid cancer. Stable disease was identified in 22 patients. Foretinib pharmacokinetics increased linearly with dose. Pharmacodynamic evaluation indicated inhibition of *MET* phosphorylation and decreased proliferation in select tumor biopsies at submaximal doses. Foretinib (formerly XL880) was developed as a small-molecule receptor tyrosine kinase inhibitor. Foretinib has nanomolar *in vitro* and *in vivo* inhibitory activity for Met and VEGF receptor-2 (VEGFR2) but it also has high *in vitro* affinity for platelet-derived growth factor receptor-β (PDGFRβ), Tie-2, RON, Kit, and FLT3 and kinases.

Foretinib caused tumor hemorrhage and necrosis in human xenografts within 2 to 4 hours.

Because preclinical toxicities associated with foretinib were generally reversible with no evidence of tumor regrowth during off-drug periods.

Taken from:

Eder JP, Shapiro GI, Appleman LJ, Zhu AX, Miles D, et al. A Phase I Study of Foretinib, a Multi-Targeted Inhibitor of c-Met and Vascular Endothelial Growth Factor Receptor 2. *Clin Cancer Res.* 2010;16(13):3507-16.

Chemotherapy-induced activation of ADAM-17: a novel mechanism of drug resistance in colorectal cancer

The exposure to anticancer drugs can trigger the activation of human epidermal receptor survival pathways in colorectal cancer (CRC). Chemotherapy (5-fluorouracil) treatment resulted in acute increases in transforming growth factor-alpha, amphiregulin, and heregulin ligand shedding in vitro and in vivo that correlated with significantly increased ADAM-17 activity. The overexpression of ADAM-17 significantly decreased the effect of chemotherapy on tumor growth and apoptosis. Pharmacologic inhibition of ADAM-17 in conjunction with chemotherapy may have therapeutic potential for the treatment of CRC.

Taken from:

Kyula JN, Van Schaeybroeck S, Doherty J, Fenning CS, Longley DB, Johnston PG. Chemotherapy-induced activation of ADAM-17: a novel mechanism of drug resistance in colorectal cancer. *Clin Cancer Res.* 2010;16(13):3378-89.

The Academy of Studenica celebrates 800 years of the Serbian medicine

From 9th to 12th June 2010, in the monastery of Studenica, under the blessings of His Holiness, the Patriarch of Serbia Mr. Irinej and the bishop of Žiča, Highly Sacred Mr. Chrizostom, the Section for history of medicine of the Serbian Medical Association and the Oncology Institute of Vojvodina from Sremska Kamenica successfully held the 15th Academy of Studenica under the name: "800 years of Serbian medicine".

"We are, as I say to you dear Irinej, foreordained by the destiny to be the east in the west and the west in the east." – wrote the Holy Sava, in his ascetic script in Karea, where the Hilandar program was created. „Thus, we command that a cell must be chosen. The cell, that is successful by its foundation. A hospital and beds must be laid before the diseased for healing and resting, and they must be given a worker to help them in any of their needs. The abbot must always, not rarely, come to the hospital and visit the brothers with zeal and bring to each of them anything that they need." After that, the Studenica program was founded, which was valid for all of the Serbian hospitals from Studenica to Jerusalem. It was not easy to "cover" thematically the whole period of these 800 years. The doctors of different specialties spoke. But, also those who are not doctors, students mingled with the professors, per *natural order* and topics, and not per *rank*. The gathering was monitored with the intense attention but also with several tears. Do the Serbs really have such *historical cultural background*? Did they really have such *colossuses*? And everything, "mercilessly" disseminated through the thickest possible scientific sieve!

The ceremonial opening of the 15th Academy of Studenica started with a prayer for the Serbian people in the King's Church, and it was continued in the dining room of the Holy Sava by the welcoming speech of PhD Vladimir Baltić, the President of the Academy of Studenica. An artistic program followed. The Academy of Studenica charters were awarded. This years winners were: MD Slavica Žižić Borjanović; a member of the Serbian Academy of Science and Arts, PhD Radoje Čolović; PhD Brana Dimitrijević, the President of the Section for history of medicine of the Serbian Medical Association and the President of the Scientific Board of this Academy; PhD Slobodan Đorđević, a lifelong honorable President of the stated Section, and the professors from Novi Sad MD Jovan Maksimović and MD Dušan Lalošević.

The program was divided into three parts: Serbian medieval medicine, Development of modern medicine in Serbia and Free topics. There were 33 lectures. Two documentary movies were displayed: "The legend of

Dragomanci" and the "Less known medicinal springs and chancels of the Fruška Gora mountain".
This gathering proved to what extent (not only) the doctors are thirsty of their own history.

Slavica Žižić-Borjanović

Report on the 21st Meeting of the European Association for Cancer Research, 26th – 29th June 2010, Oslo, Norway

21st EACR Congress was held in the premises of the *Norway Exhibition & Convention Center in* Lillestrøm, Oslo. This Congress covered all the most current topics in oncology, which may be summarized in four major themes: general, molecular and genetic epidemiology, translational research, experimental and molecular therapeutics, and pharmacogenomics and tumor immunology. The Congress' lectures were held simultaneously in three congress halls and they included special lectures of experts, educational lectures, plenary lectures that were held by the awarded lecturers, and thematic symposiums. The Congress began on 26th June, 2010, early in the afternoon, and the first lecture, the *Mühlbock lecture*, was held by the Nobel Prize in Medicine winner for the year 2009, *E. H. Blackburn* on the role of telomeres and telomerase in healthy and diseased people. The opening ceremony was held on the same day in the Oslo Opera House where, *D. Lane* held a lecture on cancer prevention as a challenge for the scientists and the society. Special attention was dedicated to molecularbiology of the tumor at the genetic (oncogenomics, non-coding RNA, genomic stability, expression and gene regulation) and the epigenetic levels. Two lectures and a special symposium were dedicated to the importance of epigenetic changes for understanding of the tumor biology and their importance for tumor diagnostics and therapy as well as for designing of new medications. The significance of microenvironment for biological behavior of the tumor was stressed out. Two expert lectures and one symposium were dedicated to tumor stem cells and the controversies related to this topic. Within the symposium on tumor chemoprevention, researches related to the role of nutrition in malignant tumor prevention were presented. Tumor biology included different aspects: mechanisms of migration, invasion and metastasizing, the significance of hypoxia and angiogenesis, cancer signaling paths and energy metabolism of a tumor cell. Immunological tumor aspects were dealt with within the symposium on immunotherapy and symposium on inflammation and cancer. Apart from lectures, there were also 250 posters. At the Congress, I presented the paper poster under the title: *The effects of proanthocyanidins on cardiotoxic and antitumor activity of doxorubicin*. The paper was presented in the section *Experimental/Molecular Therapeutics, Pharmacogenomics*. There were 90 posters within this section. The paper was received well, attracting attention because of the complexity of the approach and the possibility of implementation in people.
The Congress was well organized and more than 1500 participants were registered. Next EACR Congress shall be held in Barcelona in 2012.

Gordana Bogdanović