Odsek za molekularne in biomedicinske znanosti IJS
& Oddelek za biologijo BF UL vabita na predavanje:

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Crossroads of cancer and spermatogenesis: MAGE cancer-testis antigens evolved to protect mammalian germ cells under stress

Predavanje bo v ponedeljek, 1. julija 2019 ob 10:00
v Kolarjevi predavalnici Instituta »Jožef Stefan«,
Jamova 39, Ljubljana

Robust gamete production even in the face of environmental stress is of utmost importance for species survival, especially in mammals that have low reproductive rates. We found that melanoma antigens (MAGEs) evolved in eutherian mammals to provide protection against stress to germ cells and are hijacked by cancer cells. MAGE proteins are regulators of E3 ubiquitin ligases that are normally restricted to expression in the testis but are often aberrantly activated in cancer. We found that depletion of Mage-a genes disrupted spermatogonial stem cell maintenance and impaired germ cells transplantation efficiency. Exposure of Mage-a knockout mice to genotoxic stress or long-term starvation that mimics famine in nature caused defects in spermatogenesis and reduced fertility. Finally, human MAGE-As are activated in many cancers where they promote metabolic plasticity and confer resistance to metabolic stress. These results suggest that mammalian-specific MAGE genes evolved to ensure reproductive success under non-optimal conditions and are co-opted by cancer cells.

VABLJENI!