P68 Coexpression of Skp2 and Slug in advanced prostate cancer

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Introduction & Objectives: Skp2 is a substrate recruiting component of E3 ubiquitin-ligase complex, while Slug is a transcriptional repressor involved in epithelial-mesenchymal transition. Skp2 plays an important role in prostate cancer progression, e.g. via recently reported stabilization of EZH2 or Twist1, however, relationship with Slug needs further elucidation.

Materials & Methods: Prostate cancer patients cohort (N=101) was analysed by immunohistochemistry for the following proteins (Skp2, Slug, AR, Ki-67 and E-cadherin). Colocalization analysis was performed using Perkin Elmer Opal Multiplex kit, Vectra 3.0 imaging system and confocal microscope Carl Zeiss LSM 780. Prostate cancer PC3 cells were treated with a SCF^{Skp2} E3 ligase inhibitors (MLN4924 and SZL-P1–41) and analysed by western blot.

Results: High Gleason score was significantly associated with higher Skp2 and lower E-cadherin expression ($p<0.001$ and 0.011, respectively). Skp2 slightly correlated with Slug and AR in the whole cohort (Rs 0.32 and 0.37, respectively), which was enhanced in patients with high Gleason score (Rs 0.56 and 0.53, respectively) or with metastasis to lymph nodes (Rs 0.56 and 0.37, respectively). Confocal microscopy revealed colocalization of Skp2 and Slug in prostate cancer cells. Chemical inhibition of Skp2 by MLN4924 upregulated p27 and decreased Slug expression which supports a possible link between Skp2 and Slug proteins. Effects of SZL-P1–41 were less pronounced.

Conclusions: Immunohistochemistry, colocalization studies and in-vitro experiments support association between Skp2 and Slug in aggressive prostate cancer.

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