SNP-Array High Resolution Cytogenetic Analysis of Resectable and Advanced Pancreatic Cancer

Marina Macchini¹, Annalisa Astolfi², Riccardo Casadei³, Claudio Ricci³, Valentina Indio², Silvia Vecchiarelli¹, Marielda D’Ambra³, Elisa Grassi¹, Donatella Santini⁴, Carla Serra⁵, Raffaele Pezzilli⁵, Francesco Minni³, Guido Biasco¹, Mariacristina di Marco¹

¹Department of Oncology, ²“G. Prodi” Cancer Research Center, ³Department of Surgery, ⁴Department of Pathology, ⁵Department of Internal Medicine; Sant’Orsola-Malpighi Hospital. Bologna, Italy

Context Pancreatic cancer (PC) is the fourth leading cause of cancer deaths. The molecular mechanisms involved in the high tumorigenicity of PC are not yet well-known. Methods Pancreatic tumor samples from 14 patients were collected by ultrasound-guided biopsy and used for DNA extraction. High resolution copy number analysis was performed on Affymetrix SNP array 6.0 and analyzed with segmentation algorithm against a reference of 270 Ceu HapMap individuals (Partek Genomic Suite). Results Nine out of 14 patients exhibited both macroscopic and cryptic cytogenetic alterations, with a mean of 10 copy number alterations (CNA) per patient, while 5 patients did not show any copy number gain or loss. Deletions outnumbered amplifications by more than 2 folds. The chromosomes showing more copy number gains were chromosomes 12, 18, 19, while chromosomes 6, 9, 17 and 18 were most frequently deleted. In particular, deletions on 9p21 encompassed CDKN2A and 2B tumor suppressor genes, that on chromosome 18q21 overlapped with SMAD4, the one on chromosome 6p21 included RUNX2, while TP53 and MAP2K4 were the target genes deleted on chromosome 17p13. Amplified regions on chromosome 12p12 encompassed KRAS and ETV6 genes, the one on chromosome 18q11 overlapped with GATA6, while that on 19q13 included AKT2. We observed that the number of alterations correlates with the clinical course, and in particular that patients with none to few alterations (≤6) showed a median time to disease progression and a median overall survival significantly longer than those having a high number of CNA (>6), with a time to disease progression of 13.7 vs. 4.1 months (P=0.015) and an overall survival of 14.6 vs. 4.8 months (P=0.035). Conclusions High resolution cytogenetic analysis by SNP-array has the potential to uncover the genetic alterations carried by pancreatic tumors, and find new markers related to patient prognosis.