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Disbalance of the Mesothelin and Mucin 16 (CA125) system in pancreatic disorders

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Despite proven overexpression and known pro-malignant properties, MSLN failed an establishment as a target or marker in pancreatic cancer. Our study was first to take MSLN/MUC16 as a system and reveal its disbalance in pancreatic diseases in general and pancreatic tumor cells in particular. Comprehensive analysis of pancreatic and systemic MSLN and MUC16 levels in a panel of inflammatory, benign and malignant disorders, allowed us to elucidate diagnostic value of the intrapancreatic changes as well as uncoupling and prognostic relevance of systemic alterations. 'Over-mesothelinization' emerged as a syndrome accompanying any pancreatic disorder; more selective MUC16-overload showed stronger association with a malignancies. Abundance of shed isoforms, systemic or intratumoral, might represent a major obstacle for MSLN-targeted therapies and also should be explored for immunosuppressive consequences. The identity of pancreatic factors, released into circulation and promoting shedding of sMSLN and sMUC16 at remote extra-pancreatic locations, remained to be determined. Our data suggested that only 25% of tumor cells permit an autocrine MSLN/MUC16 signaling, but all of them overexpress pathway's downstream target, NBPF10. Nevertheless, the suitability of this little-studied NBPF-family of nuclear proteins as MSLN/MUC16's 'replacement' marker/target is questionable.