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USING HIGH-DENSITY PROTEIN MICROARRAYS TO DEFINE A MOLECULAR SIGNATURE OF AUTOANTIBODIES IN COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is the most abundant type of neoplasia in developed countries and the second cause of death among cancers due mainly to a late diagnosis. Cancer proteins elicit an immune response in the host. Then, the autoantibody repertoire from cancer patients might serve to identify tumour-associated antigens (TAAs) that could be used as biomarkers for diagnosis and prognosis.

Experimental procedures: Protoarray was used to identify TAAs as potential biomarkers using 8 serums from normal individuals and 12 colorectal cancer patients. Western blotting analysis with seven CRC cell lines and normal and tumoral tissue extracts was performed with antibodies against 3 differentially expressed TAAs. A specific CRC tissue microarray was tested with an antibody against one of these differentially expressed proteins. Thirty-five serum from colorectal cancer patients and 23 from healthy individuals were tested by ELISA with 4 purified antigens.

Results: A preliminary autoantibody signature specific for CRC has been identified. We have verified by immunoblotting the differential reactivity of three of those proteins. Pim1 and MAPKAPK3 were more abundant in tumoral samples, whereas ACVR2B was decreased. We have also validated by tissue microarray the absence of ACVR2B in colon tumoral samples. Finally, to determine the discrimination capacity between normal and tumoral groups, we tested 58 serum samples by ELISA using the purified antigens and constructed the ROC curves. Applying statistical models, the combination of Pim1 and ACVR2B exhibited a specificity and sensitivity of 71,4% and 77,1% to discriminate between groups.

Conclusions: Protein microarrays as novel high-throughput proteomic approaches have accelerated the interest in human serum autoantibodies against cancers for the discovery of candidate TAAs to be used as specific tools to diagnose cancer. We have identified a set of potential biomarkers for CRC diagnosis and also as potential immunological therapeutic targets that is being currently evaluated.