madridge CONFERENCES
3rd International
Cancer Study & Therapy Conference
May 2-4, 2018 Rome, Italy

Anti-FIRs (PUF60) Auto-Antibodies were Detected in the Sera of Early-Stage Colon Cancer Patients. Identification of Specific and Common Diagnostic Antibody Markers for Gastrointestinal Cancers by SEREX Screening Using Testis cDNA Phage Library

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Anti-PUF60, poly(U)-binding-splicing factor, autoantibodies are reported to be detected in the sera of dermatomyositis and Sjogren's syndrome. PUF60 is identical with far-upstream element-binding protein-interacting repressor (FIR) that is a transcriptional repressor of *c-myc* gene. In colorectal cancers, a splicing variant of FIR that lacks exon2 (FIRΔexon2) is overexpressed as a dominant negative form of FIR. The autoantibodies for FIRs were examined in the sera of 87 colorectal cancer patients. Anti-FIRs antibodies were surely detected in the preoperative sera of 28 colorectal cancer patients (32.2% of positive rates), and the detection rate was significantly higher than that in healthy control sera by Alpha (amplified luminescent proximity homogeneous assay)-LISA assay. The level of anti-FIRs antibodies significantly decreased after the operation. Furthermore, the area under the curve of receiver operating characteristic for anti-FIRs antibodies was significantly larger (0.85) than that for anti-p53 antibodies or CA19-9. In conclusions, Anti-FIRs antibodies were detected in relatively early-stage colorectal cancers.

Further, we have screened autoantibodies by phage expression cloning and identified novel fourteen antigens. As for auto-antibodies against fourteen antigens, Alpha-LISA assay was performed in the sera of gastrointestinal cancers patients to confirm the results. Serum antibody levels against these fourteen recombinant proteins as antigens between healthy donors (HD) and esophageal squamous cell carcinoma (ESCC) patients, gastric cancer (GC), or colon cancer (CC) were compared. Receiver operating curve (ROC) revealed similar results except CCNL2 in CC. AUC values calculated by ROC were higher than 0.7 in TPI1, HOOK2, PUF60, PRDX4, HS3ST1, TUBA1B, TACSTD2, AKR1C3, BAMBI, DCAF15 versus ESCC, TPI1, HOOK2, PUF60, PRDX4, TACSTD2, AKR1C3, BAMBI, DCAF15 versus GC, and TPI1, HOOK2, PUF60 versus CC. AUC of the combination of HOOK2 and p53 antibodies versus ESCC was observed to be as high as 0.8228. Higher serum antibody levels against 10 antigens could be potential diagnostic tool for ESCC. Higher serum antibody levels against 8 antigens could be potential diagnostic tool for GC, and serum antibody levels against 3 antigens could be potential diagnostic tool for CC.

Keywords auto-antibody, cancer biomarker candidate, colorectal cancer, far-upstream element-binding protein-interacting repressor (FIR); poly(U)-binding-splicing factor (PUF60).

Biography:

Kazuyuki Matsushita in 1988 graduated from Chiba University and was awarded with MD. In 1995 maintained his PhD at the Graduate Scholl of Medicine, Chiba University in Japan. From 1997 through 2000 was a visiting fellow, of the NCI, NIH, USA. In 2015, he was listed as a Board of Laboratory Medicine, Japanese Society of Laboratory Medicine, Japanese Board of Medical Genetics, form the Japan Society of Human Genetics. In 2010, he got the Board of Specialty in Cancer Treatment from Society of Japanese Cancer Treatment Society. At present he is a Professor of Department of Laboratory medicine, Director of Laboratory Medicine, Division of Clinical Genetics and Proteomics, Chiba University Hospital, Chiba, Japan. He has been studying c-myc transcriptional regulation, especially demonstrated on c-myc transcriptional repressor FIR (FBP interacting repressor) in carcinogensis. Proteomic and genomic analysis in cancinogenesis and DNA damage repair pathway for clinical validities such as cancer treatment and diagnosis. Establishment of biobanks network of human clinical samples in Japan for novel biomarkers research are studied in his group.