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Prognostic evaluation of anoikis resistance subpopulations in colorectal carcinoma tissues and 3D *in vitro* modeling of anoikis resistance to assess impact of mutated oncogenes

Madhura Patankar
University of California, USA

Anoikis is a form of cellular apoptosis and resistance to anoikis is a known mechanism in metastatic and invasive colorectal carcinoma. Colorectal carcinoma is the third most common cause of cancer related deaths worldwide and yet, anoikis resistance assessments are limited by *in vitro* studies. To address this, we first identified and then quantified anoikis resistant subpopulation of colorectal cancer tissues and evaluated their prognostic significance. In addition, we also generated 3D *in vitro* model of anoikis resistance using colorectal cancer cell lines with mutated KRAS and BRAF oncogenes to assess association of these mutations commonly found in CRC and their role in receiving and maintain anoikis resistance ability. For histopathological evaluations, we assessed Hematoxylin and eosin staining's on tissue microarray specimens followed by IHC staining's for proliferation, apoptosis, and basement membrane markers to establish cell/s with or without anoikis resistance. Alternately we modeled this mechanism *in vitro* and generated KRASG12V and BRAFV600E Caco-2 colon cancer cells lines using retroviruses to understand role of these mutated oncogenes on cell fate. Main findings: we observed low apoptosis rate and low proliferative index in cell populations without any contact to extracellular matrix that was shown by absence of basement membrane staining. Colon cancer cells with mutated oncogenes showed interesting features with low apoptosis rate (annexin negative) and features of quiescence (G0 cell cycle arrest) by flow cytometry. Cells with mutated oncogenes when cultured in 3D cultures formed either partially or full filled cysts mimicking cribriform and solid structures noted from CRC tissues. In conclusion, we have shown evidence of subpopulations of carcinoma cells in micropapillary, cribriform, solid structures are resistant to anoikis resistance and abundance of these structures is new independent indicator of poor prognosis in CRC both in primary and metastatic lesions.

Biography

Madhura Patankar has completed her Masters in Protein Chemistry and Biotechnology from Department of Biochemistry at University of Oulu, Finland and then completed her PhD in Experimental Pathology and Cancer Biology from Department of Pathology at University of Oulu, Finland. She then moved to University of Southern California, CA and worked on mechanisms underlying inflammatory diseases such as Gastro esophageal reflux disease (GERD.). She is currently postdoctoral research at University of California Davis, CA investigating single cell signaling dynamics in perturbed metabolic pathways and mechanisms underlying lung epithelial injury and their crosstalk with stroma.

Madhura.patankar05@gmail.com

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