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GALECTIN-3, A DRUGGABLE VULNERABILITY FOR KRAS-ADDICTED CANCERS

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Identifying the molecular basis for cancer cell dependence on oncogenes such as KRAS can provide new opportunities to target these addictions. Here, we identify a novel role for the carbohydrate-binding protein galectin-3 as a lynchpin for KRAS dependence. By directly binding to the cell surface receptor integrin αvβ3, galectin-3 gives rise to KRAS addiction by enabling multiple functions of KRAS in anchorage-independent cells, including formation of macropinosomes that facilitate nutrient uptake and ability to maintain redox balance. Disrupting αvβ3/galectin-3 binding with a clinically active drug prevents their association with mutant KRAS, thereby suppression macropinocytosis while increasing reactive oxygen species to eradicate αvβ3-expressing KRAS-mutant lung and pancreatic cancer patient-derived xenografts and spontaneous tumors in mice. Our work reveals galectin-3 as a druggable target for KRAS-addicted lung and pancreas cancers and indicates integrin αvβ3 as a biomarker to identify susceptible tumors. There is a significant unmet need for therapies targeting KRAS-mutant cancers. Here, we identify integrin αvβ3 as a biomarker to identify mutant KRAS-addicted tumors that are highly sensitive to inhibition of galectin-3, a glycoprotein that binds to integrin αvβ3 to promote KRAS-mediated activation of AKT.

BIOGRAPHY

Laetitia Seguin is currently working as a post-doctoral fellow in C Feral Laboratory Epithelial homeostasis and tumorigenesis at IRCAN, France. She has published many papers in the reputed journals with the eminent authors. She has a great publication in the peer reviewed conference proceedings also.

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