Sensitized serotonin-mediated vasodilation in a mouse model of carcinoid disease

Byron Lee BS\(^1\) OMS-II, Deanna Choi MS\(^2\), Sydney Kuehn BS\(^1\) OMS-III, Sofia Penrose BS\(^1\) OMS-III, Rodney F. Pommier MD,\(^3\) Ashley E. Walker PhD\(^2\), Belinda H. McCully PhD\(^1\)

\(^1\) Department of Basic Medical Sciences, COMP-NW, Western University of Health Sciences
\(^2\) Department of Human Physiology, University of Oregon  \(^3\) Division of Surgical Oncology, Department of Surgery, Oregon Health & Science University

INTRODUCTION
Carcinoid tumors secrete vasoactive hormones such as serotonin that can impact cardiovascular function. In consequence, patients with metastatic carcinoid disease are at risk for carcinoid syndrome, characterized by profound cutaneous flushing, hypotension and syncope. This may be attributed to the vasodilatory effects of serotonin. Our recent work shows that in patients with carcinoid disease, higher serotonin levels are associated with lower vascular resistance. Whether the vasculature is sensitized to serotonin is not known.

METHODS

Animal Model: Anesthetized (3-5% isoflurane in 100% O\(_2\)), J:Nu nude mice (25-30g) received intrasplenic injection of 2x10\(^7\) BON1 neuroendocrine tumor cells (BON1, n=5) or PBS-vehicle (VEH, n=5), and monitored for 10 weeks for the development of liver carcinoid metastases.

Ex vivo vascular function: Mesentery arteries were cannulated onto glass pipette tips, pressurized, and incubated in a physiological salt solution at 37°C in an organ chamber bath. After equilibration, vessels were pre-constricted with phenylephrine, and dose response curves were generated to assess serotonin-mediated vasodilation.

RESULTS

(A) VEH and BON1 mice exhibited a dose-dependent increase in serotonin-mediated vasodilation. (B) The maximal vasodilatory response to serotonin was significantly higher in BON1 mice (65 ± 6%) compared to VEH (44 ± 8%, p<0.05).

CONCLUSIONS

1) Serotonin-mediated vasodilation is sensitized in a mouse model of carcinoid disease.

2) Serotonin-mediated vasodilation is accompanied by enhanced \(\alpha\)-adrenergic-mediated vasoconstriction, which may be a compensatory mechanism in response to sensitized vasodilatory mechanisms.

HYPOTHESIS
We hypothesized that serotonin-mediated vasodilation is increased by carcinoid metastases.

ACKNOWLEDGEMENTS
• COMP-NW: Anna Breen BS, Ariana Cast BS, Willie Bidot DVM
• University of Oregon: Walker Laboratory
• Funding: Western University of Health Sciences Intramural Grant (McCully)
• BON1 cells provided by Dr. Katalin Modis – University of Texas Medical Branch at Galveston.