



Asael Roichman, PhD

Princeton University



TECHNION
Israel Institute
of Technology

rticc
Rappaport
Technion Integrated Cancer Center

*Cancer
Cure is
Born Here*



D. DAN AND BETTY KAHN
HUMAN HEALTH BUILDING

RTICC SEARCH COMMITTEE SEMINAR

9th July
12:00-13:00



**4th Floor seminar Room, The Ruth and
Bruce Rappaport Faculty of Medicine**

- Light refreshments will be served

“The Interplay between Diet, Gut Microbiota and Cancer Therapy”

Diet can profoundly influence cancer therapy, yet the mechanisms linking specific dietary components to therapeutic efficacy remain unclear. To investigate this, I studied phosphatidylinositol 3-kinase (PI3K) inhibitors, which show limited efficacy in human solid tumors. In murine models, PI3K inhibitor activity is dramatically enhanced by a ketogenic diet, previously attributed to dietary suppression of insulin. I confirmed this enhancement but surprisingly found it to be unrelated to diet macronutrient composition, glycemia, or insulin. Instead, the diet–PI3K interaction involves microbiota metabolism of ingested phytochemicals. Specifically, the murine ketogenic diet is a purified formulation that lacks the complex spectrum of phytochemicals present in standard chow, including the soy phytochemicals soyasaponins. These compounds are converted by the gut microbiota into inducers of hepatic cytochrome P450 enzymes, which accelerate PI3K inhibitor clearance and reduce drug efficacy. A high-carbohydrate, low-phytochemical diet, as well as antibiotics that suppress the gut microbiota, enhance PI3K inhibitor activity in mice. These findings reveal a phytochemical–microbiota–liver axis that modulates systemic drug levels and efficacy. I also examined whether dietary fiber enhances immune checkpoint blockade (ICB), as suggested by clinical studies, and found that fiber content alone had limited and inconsistent effects on ICB efficacy across tumor models—suggesting that other dietary factors correlated with fiber intake, possibly phytochemicals, may underlie observed clinical associations. These studies highlight the importance of considering dietary phytochemicals and microbiota when evaluating drug exposure, therapeutic efficacy, and inter-individual variability in treatment response.