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Cancer-related pathway reveals potential treatment target for rare pediatric disease

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Cancer researchers studying genetic mutations that cause leukemia have discovered a connection to the rare disease cherubism, an inherited facial bone disorder in children.

The link is the enzyme Tankyrase and its pivotal role in switching on or off the protein that controls two known cancer genes. In normal cells, the protein is vital for bone development. In abnormal cells, it is thought to be involved in two common types of blood cancer – chronic myelogenous leukemia and acute myeloid leukemia.

The findings, published online today in *Cell*, zero in on how the enzyme alters the protein 3BP2, says principal investigator Dr. Robert Rottapel, clinician-scientist at The Campbell Family Institute for Cancer Research in the Princess Margaret Cancer Program, University Health Network and St. Michael's Hospital. He is also a Professor, Faculty of Medicine, University of Toronto, and holds the Amgen Chair for Cancer Research.

"We have defined the rules of engagement for Tankyrase, which clearly identifies a potential target for developing therapeutic agents for human disease," says Dr. Rottapel. These studies point the way for new therapeutic approaches in treating cherubism, using inhibitors that are already available in the clinic.

In a separate but related study (also published today) co-led by Dr. Rottapel and Dr. Frank Sicheri at the Samuel Lunenfeld Research Institute, Mount Sinai Hospital, the investigators further defined the

structural details that define the interaction between Tankyrase and 3BP2.

"Tankyrase sits in the nexus of several known cancer pathways. These studies have helped us discern its role and have opened the door to a whole new area in how information is processed in cells that was previously obscure. We have furthered our understanding of how genes that control development often control cancer," says Dr. Rottapel.

He adds: "This is how research happens; following unanticipated opportunities that unveil connectivity that teaches us about the general pathways that lead to human disease."

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