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Trickery at the Cellular Level

Focus: To identify new and unexpected therapeutic targets for the treatment of acute myeloid leukemia (AML).

Albert Einstein said, “The most beautiful thing we can experience is the mysterious. It is the source of all true art and science.” Dr. Sykes is indeed working with a beautiful mystery. He has found a way to trick leukemia cells into maturation by inhibiting the enzyme dihydroorotate dehydrogenase (DHODH) within those cells. The reason this occurs is not clear, but the implication certainly is: people with AML could receive a treatment dramatically superior to what has been a mostly unmodified standard of care for more than four decades.

“Any interruption in the balance of cells being created and cells dying leads to an accumulation of immature cells that no longer respect that normal process,” Dr. Sykes says. “Cancer cells are not inherently malicious—they are simply confused, stuck in an immature state. Traditionally we have killed immature cells with chemotherapy, with its expected side effects. With help from Harrington we are building upon this foundation of differentiation therapies to find targets beyond DHODH that will set those cells back into the normal process of development.”

“This work is focused on AML, but we are also exploring how the concept of differentiation therapy and how these molecules in particular might be able to address other cancers, and in particular other solid tumor malignancies,” Dr. Sykes says.

Impact Wish:

“Imagine a well-tolerated drug that spares normal cells while specifically promoting the maturation of leukemia cells. In other words, imagine a superior alternative to chemotherapy.”