Researcher to cancer: 'Resistance will be futile'

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Borden, principal investigator at IRIC and professor at the University of Montreal's Department of Pathology and Cell Biology, Zahreddine and their colleagues have in fact uncovered a previously unknown form of multidrug resistance, known as inducible drug glucuronidation. "We discovered this form of resistance when we developing a means to target a specific cancer-causing gene known as elF4E with a drug called ribavirin. Ribavirin prevents some viruses from reproducing their genetic code, and it has been used in two clinical studies to successfully to attack some cancers. However, all patients eventually relapsed," Borden explained. "We found that this was because cancer cells metabolize drugs differently from each other as well as normal cells. We traced the chemical pathway responsible for the decreased sensitivity to the drug to a protein that governs the copying of genetic information. We were able to shut off the protein and restore sensitivity to the ribavirin, and also to Ara-C, another cancer drug that cancer cells were able to defend themselves from by evolving."

The findings are the first step on a great voyage into the unknown. "It

seems likely that each cell is able to develop resistance to multiple drugs. Moreover, it is likely that glucuronidation is not the only inducible modification, and finally, that this process can be very rapid, occurring even within weeks," Borden explained. "I'm a cancer researcher, not a doctor, but I'll boldly declare that the findings aren't bad news for those of us who want to live long and prosper. By understanding the extent of these inducible modifications and the chemical pathways that make their assimilation possible, it's a question of when, not if, we will finally be able to tell cancer cells that resistance is futile."

More information: Katherine L. B. Borden, "When Will Resistance Be Futile?" in *Cancer Research*, December 4, 2014.
Borden, Hiba Zahreddine, et al. "The sonic hedgehog factor GLI1 imparts drug resistance through inducible glucuronidation", *Nature*, May 28, 2014.

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