# Overcoming multidrug resistance in acute lymphoblastic leukemia cells

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A strong predictor of poor outcome in children with acute lymphoblastic leukemia (ALL) is resistance to chemotherapy with glucocorticoids. Such resistance is caused, in part, by an inability of the leukemic cells to die by a process known as mitochondrial apoptosis. However, researchers have now identified a way to get round this block in mitochondrial apoptosis in glucocorticoid-resistant childhood ALL cells.

Acute lymphoblastic leukemia (ALL) most commonly affects children, in whom there is an overall cure rate of 85%. A strong predictor of poor outcome is resistance to chemotherapy with glucocorticoids. Such resistance is caused, at least in part, by an inability of the leukemic cells to die by a process known as mitochondrial apoptosis. Many researchers are therefore trying to find ways to overcome the block in mitochondrial apoptosis in glucocorticoid-resistant leukemic cells. Jean-Pierre Bourquin and colleagues, at the University of Zurich, Switzerland, have now identified a way to do just that, showing that this approach resensitizes multidrug-resistant childhood ALL cells to glucocorticoids and other cytotoxic agents.

The authors found that treating multidrug-resistant childhood ALL cells with the drug obatoclax, which is under development for the treatment of both cancer and leukemia, resensitized them to glucocorticoids and other cytotoxic agents. Further analysis indicated that this reversal of glucocorticoid resistance occurred through rapid activation of a process known as autophagy-dependent necroptosis, bypassing the block in mitochondrial apoptosis.

As the levels of obatoclax required to achieve these effects were not themselves toxic to the cells, the authors suggest that their data provide the rationale for treating individuals with multidrug-resistant ALL in a similar way.

**More information:** Induction of autophagy-dependent necroptosis is required for childhood acute lymphoblastic leukemia cells to overcome glucocorticoid resistance, www.jci.org/articles/view/3998 … 4e895dead848910ba5a2

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