

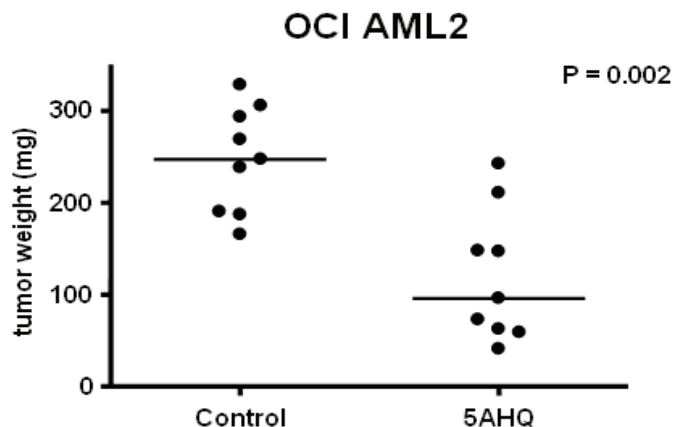
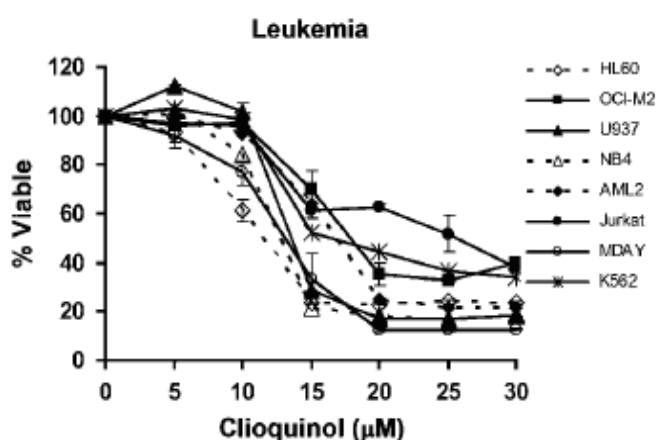


Clioquinol Analogues for Treatment of Lymphoid Malignancies

Overview of Technology:

Acute myeloid leukemia (AML) and multiple myeloma (MM) are malignant diseases resulting in the proliferation of abnormal cells of myeloid and lymphoid origin, respectively. Both diseases are characterized by poor responses to standard therapies. For example, elderly patients with either AML or myeloma and poor risk cytogenetics have a median survival of less than one year. Thus, for these patients and those with relapsed refractory disease, novel therapies are needed. As many of these patients are frail, therapies that achieve an anti-myeloma or anti-leukemia effect without significant toxicity are highly desirable.

A high throughput screen identified several clioquinol analogues acting as inhibitors of cyclin D2 transactivation, which is over-expressed in patients with high risk AML and MM. The compounds were subsequently shown to inhibit the proteasome through copper dependent and independent mechanisms. Further, the researchers demonstrated that this parent compound and analogs thereof, such as 5AHQ, DHQ, HNQ, BCQ, COQ, 8HQ and diiodoQ, induce cell death in hematological malignancies including multiple myeloma and leukemia cells.



The use of clioquinol analogues provide novel treatments for proliferative diseases involving increased expression of D-cyclins and/or hematological malignancies, such as leukemias including AML, MM, and acute lymphocytic leukemia (ALL).

Related Publications:

Mao, X. *et al.* Clioquinol inhibits the proteasome and displays preclinical activity in leukemia and myeloma. *Leukemia*. **23**, 585-590 (2009)

Mao, X. and Schimmer, A.D. The toxicology of Clioquinol. *Toxicology Letters*. **182**, 1-6 (2008)

Patent:

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