



Treating Cancer with Statins and Dipyridamole

Overview of Technology:

The statin family of drugs target HMG-CoA reductase, the rate-limiting enzyme of the mevalonate pathway, and have been used for decades in the treatment of hypercholesterolemia. Research has shown that statins trigger tumor cells to undergo apoptosis without damaging normal cells. To increase statin efficacy as anti-cancer agents a UHN research group led by Dr. Linda Penn, recently conducted a screen to identify off-patent, FDA-approved agents that can potentiate atorvastatin-induced apoptosis of tumor cells. To this end, the Linda Penn's lab collaborated with UHN researcher, Aaron Schimmer's lab who have accrued small molecule libraries of these agents. The UHN collaborative research helped identify dipyridamole as potentiating the anti-proliferative activity of atorvastatin in a screen conducted on a cell line (KMS11) derived from multiple myeloma (MM). The UHN researcher's further showed that atorvastatin and dipyridamole synergize to kill a variety of cell lines derived from acute myelogenous leukemia (AML) as well as MM. Furthermore, this synergy is not restricted to atorvastatin as it is also evident with fluvastatin and dipyridamole, suggesting the entire statin class of drugs can be used with dipyridamole to synergistically kill tumor cells. This tumor cell death occurs through the process of apoptosis suggesting this combination of agents will kill tumor cells by a non-inflammatory mechanism of action.

Evidence shows that atorvastatin and dipyridamole can potentiate apoptosis of primary patient AML cells. Efficacy of atorvastatin alone is shown in an animal xenograft model of MM cells (KMS11). Doses of atorvastatin and dipyridamole that are themselves not able to function as antiproliferatives have been established and these are now undergoing evaluation as combination therapy in this animal model in vivo. Dipyridamole (commercially known as Persantine) is used in the control of recurrent stroke and is widely prescribed as a vasodilator and inhibitor of platelet aggregation. It is anticipated this combination of agents will advance to clinical trials in the near future, in which to evaluate adverse reactions as well as efficacy as anticancer agents. This combination has potential to be efficacious against all cancers, as is described within the US provisional that has been filed.

Related Publications:

Publication and additional information available under a CDA as has yet to be released.

Patents:

US61/294,685 and US61/294,691 - Filed Jan 10, 2010

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