The drug pirbuterol, a beta 2 adrenergic receptor (β2AR) agonist inhibits the Raf-1/Mek-1/Erk1/2 pathway by decreasing levels of phospho-Erk1/2 (P-Erk1/2). In xenograft mice, pirbuterol resulted in tumor regression, and when these mice were taken off the pirbuterol, none of the tumors regrew and the tumors remained undetectable. Pirbuterol itself has data to suggest it may be safely administered to humans because an inhalable version is FDA-approved for asthma, and the drug was administered orally to humans in studies of congestive heart failure. 30% of the NCI-60 cell lines exhibit high amounts of both β2AR and P-Erk1/2 suggesting various cancers may respond to pirbuterol.

COMMERCIAL OPPORTUNITY

- There is potentially a large market for pirbuterol as a novel anticancer therapy, given that 30% of the NCI-60 cell lines exhibit high amounts of both β2AR and P-Erk1/2 including colon, CNS, leukemia, lung, breast, ovarian and renal cancer cell lines.
- The markets for these cancers are large as suggested by the number of new cases each year and the estimated deaths where current treatments were unsuccessful. The US estimated new cases and deaths in 2014 for each category are colon (96,830 new, 50,310 deaths), CNS (23,380 new, 14,320 deaths), leukemia (52,380 new, 24,090 deaths), lung (224,210 new, 159,260 deaths), breast (235,030 new, 40,430 deaths), ovarian (21,980 new, 14,270 deaths) and renal (63,920 new, 13,860 deaths).
- Targeting this pathway has led to approved Raf and Mek inhibitors. The Raf inhibitors include Tafinlar (estimated global revenue of $371 million by 2017) and Zelboraf ($250 million globally in 2012) that are currently marketed for treating melanomas that have a mutant BRAF kinase. The Mek inhibitors include Trametinib (GSK1120212), a MEK1 and MEK2 inhibitor that is also FDA-approved to treat BRAF mutant melanomas, as well as MEK inhibitors in development, including Selumetinib for lung cancer, MEK162 for biliary tract cancer and melanoma, and PD-325901 for breast, colon, and melanoma.

TECHNOLOGY

The small molecule agonist of β2AR, ARA-211 (Pirbuterol), causes tumor regression by inducing production of cAMP through the β2AR, which activates Protein Kinase A to block hyperactivated Raf-1/Mek-1/Erk1/2 pathway signaling. Pirbuterol has been tested in pre-clinical mouse xenograft models of various cancers, with the strongest effects occurring in breast and renal tumor models. Upon treatment with 100mg/kg Pirbuterol, MDA-MB-231 breast xenografts stopped growing and with 200mg/kg pirbuterol, the xenografts shrunk to an undetectable size. 200mg/kg pirbuterol completely halted renal cancer cell xenograft (ACHN) growth as well. Three additional weeks after stopping treatment, neither the breast nor renal tumors resumed growing in the mice, indicating a lasting effect on tumor growth.

PUBLICATION/PATENT