



Drug Delivery and Targeting with Vitamin B12 Conjugates

Principal Investigator:
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Background:

Vitamin B12 (cyanocobalamin) is an essential cofactor for DNA replication and cell division. Thus, rapidly dividing cells require greater amounts of vitamin B12. Tumor cells, in particular, tend to produce from about 100 to 1000 times the number of receptors for vitamin B12 and up to fifty times more of its carrier protein, transcobalamin II (TCII).

Description of Project:

Taking advantage of their greater need for this cofactor, Dr. Wilson's laboratory has designed a system to employ vitamin B12 for selective delivery of drugs to tumors. Hydrolysis of vitamin B12 leads to three major monocarboxylic acid isomers (known as b, d, and e). They coupled 4,7,10-trioxa-1,13-tridecanediamine (as a linker between B12 and drug) to each and have performed TCII binding studies. Conjugation at the e-position did not substantially affect the binding of B12 to TCII. For example, it was shown that B12 linked to p-iodohippurate bound to TCII almost as well as B12 alone, and was found to be bioactive. They were then able to attach various therapeutic agents to the B12-linker compound and evaluate their anti-cancer activity. The primary advantage of this delivery system would be the ability to lower the dosage, and therefore the accompanying collateral damage to healthy tissues, of current therapeutic compounds.

Applications:

- 1) Vitamin B12 can be conjugated to anti-cancer drugs in order to deliver them more selectively to tumors.
- 2) Selective delivery of drugs to rapidly dividing cells in disorders such as rheumatoid arthritis, severe psoriasis, and neoplastic diseases,

Patent Status:

A non-provisional US patent application has been filed.

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