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Synthesis of Metal-Containing Polymers to Combat Cancer

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Cancer is the number one disease that takes human life. It often does so in an elongated manner beginning in several cells but eventually taking over the body rendering the occupant unable to cope with the results.

Why is the polymeric form of our drugs advantageous in fighting cancer. These are briefly described as follows. The large size aids in the retention of the polymer-drug. It increases retention time allowing more time for the drug to take effect. Polymers are filtered by the kidney more slowly reducing kidney damage. There is also a greater ability for binding to the target. The large size allows for more than a single drug to be carried by the polymer allowing for more modes of anticancer activity. Additionally, polymers can have the ability to behave as a prodrug allowing them to enter the cell in an inactive form and slowly degrade into an active form inside the cell. The slow degradation of the polymer into the active form can be thought of a sort of time release drug. Large molecules, like polymers, may have the ability to collect to a greater extent in solid tumors compared to healthy tissues due to the fact that tumors have limited lymphatic drainage therefore, the polymer drug is able to be built up in the tumor. This effect of the polymers collecting in the tumors is known as the enhanced permeability and retention (EPR) effect. Polymeric drugs also have the advantage of greater design possibilities compared to a monomeric drug. Polymers may be synthesized with specific characterizations, chain length, polarity, monomeric components, and cross-linking allowing polymers the possibility to maximize their anticancer activity. aFinally, polymers may be coupled to molecules that have the ability to target a specific transport mechanism. The coupling of these molecules can be used as an escort to transport the polymer drug to a specific site without influencing the drugs activity.

Previously we focused on a series of phosphorus polymers based on nucleic acid-like structures [1-7]. Recently, we focused on metal-containing polymers due to their propensity for the biological inhibition of viruses, bacteria, fungi, and cancer metal atoms incorporated into these biologically active polymers. Examples of these metals include tin [8-22], Group 4 and 5 metallocenes [23-30], platinum [31-33] and Group 15 metals, namely arsenic, antimony, and bismuth [31-40]. The metal-containing polymers listed in references [8-30], all showed good inhibition these cancer strains.

Because of the mild conditions offered by the interfacial polymerization system, it was chosen as the synthetic procedure [41-45]. Reactions are conducted under normal room conditions resulting in production of moderate yield and typically high chain length.

Our current focus is on brain and pancreatic cancers. The effective application of these chemotherapeutic organometallics to treat glioblastomas brain cancer is the end goal. The typical prognosis is not favorable with a five-year survival rate in the USA of about one third. In the USA there are about 44,000 new brain tumors (2005) accounting for about 2.5% of the cancer-related deaths. Presently, there is no effective chemotherapy for the treatment of glioblastomas. While the current focus is on brain cancer, the compounds may prove useful in the treatment of other brain related problems including Alzheimer's, dementia, amnesia, autism, epilepsy, stroke, Lupus, cerebral palsy, Parkinson's, etc.

Table 1: *Cancer strains*

Strain Number	NCI Designation	Species	Tumor Origin	Histological Type
3465	PC-3	Human	Prostate	Carcinoma
7233	MDA MB-231	Human	Pleural effusion breast	Adenocarcinoma
1507	HT-29	Human	Recto-sigmoid colon	Adenocarcinoma
7259	MCF-7	Human	Pleural effusion-breast	Adenocarcinoma
ATCC CCL-75	WI-38	Human	Normal embryonic lung	Fibroblast
	U251	Human	Glioblastoma multiforme	Astrocytoma
	G55	Human	Glioblastoma	Astrocytoma
	AsPC-1	Human	Pancreatic cells	Adenocarcinoma
	PANC-1	Human	Epithelioid pancreatic cells	Carcinoma

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