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Delivery of epigenetic drugs against asbestos cancer

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Several aggressive cancers such as the asbestos cancer are not correctly treated with conventional drugs. New therapeutic strategies include epigenetic modulators able to stop cancer cell growth by renormalization of their epigenetic landscape leading to apoptosis. As this epigenetic renormalization requires hours to be effective and because epigenetic drugs have short half live, the use of delivery systems is especially suited to improve the therapeutic efficacy of epigenetic treatments. We present our results in this particular application of drug delivery systems. The delivery systems presented is based on polymeric nanoparticles prepared by Ring-Opening Metathesis Polymerization (ROMP). Each macromonomer can be functionalized to access a library of functional macromonomers that are the copolymerized to generate (multi) functional 300 nm sized nanoparticles. This system is able to selectively accumulate in the tumors in subcutaneous or peritoneal mice models. The epigenetic drugs are covalently loaded and released inside cancer cells after internalization through acidic vesicles. This intracellular delivery leads to an increase of histone acetylation in the nucleus due to the delivery of inhibitors of histone deacetylases, the biological target in our strategy. The particles are not detected in other organs as well as the epigenetic effect, indicating the highly selective effect of our strategy. In a peritoneal mice model of asbestos cancer, 80% of tumor reduction was obtained when the free compounds gave no results.

Biography

Philippe Bertrand has obtained his PhD in 1992 at Poitiers University, developing asymmetric synthesis from the chiral pool. He has worked on alkaloid hydroxylation in super acids during his Postdoctoral research from 1992 until 1995. He has achieved a Lecturer position in Poitiers to develop asymmetric synthesis of anticancer compounds. He has started to work on epigenetics in 2004, developing synthetic methods to access epigenetic inhibitors and their use in delivery systems for therapeutic or imaging purposes.

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