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New scaffolds for the delivery of protease sensitive photosensitizer prodrugs

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Protoporphyrin IX (PpIX) as natural photosensitizer derived from administration of 5-aminolevulinic acid (5-ALA) has found clinical use for photodiagnosis and photodynamic therapy of several cancers. However, broader use of 5-ALA in oncology is hampered by its charge and polarity that result in its reduced capacity for passing biological barriers and reaching the tumor tissue. Advanced drug delivery platforms are needed to improve the biodistribution of 5-ALA. Here, we report a new approach for the delivery of 5-ALA. Squalenoylation strategy was used to covalently conjugate 5-ALA to squalene, a natural precursor of cholesterol. 5-ALA-SQ nanoassemblies were formed by self-assembly in water. The nanoassemblies were monodisperse with average size of 70 nm, polydispersity index of 0.12, and ζ-potential of + 36 mV. They showed good stability over several weeks. The drug loading of 5-ALA was very high at 26%. In human prostate cancer cells PC3 and human glioblastoma cells U87MG, PpIX production was monitored in vitro upon the incubation with nanoassemblies. They were more efficient in generating PpIX-induced fluorescence in cancer cells compared to 5-ALA-Hex at 1.0 to 3.3 mM at short and long incubation times. Compared to 5-ALA, they showed superior fluorescence performance at 4 h which was diminished at 24 h. 5-ALA-SQ presents a novel nano-delivery platform with great potential for the systemic administration of 5-ALA. For the first time in 5-ALA related research, these finding opens the possibility to treat patients without light.

Biography

He is affiliated from University of Geneva. He is a recipient of many awards and grants for her valuable contributions and discoveries in major area of subject research. His international experience includes various programs, contributions and participation in different countries for diverse fields of study.