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A bacteria virus that targets and destroys tumors in preclinical models

Amin Hajitou
Imperial College London, UK

Despite their attractive features and advanced knowledge of their molecular biology, bacteriophages (phage) are still considered poor vectors for gene transfer limiting their application in a range of disciplines including gene therapy and DNA vaccine delivery. Phage has evolved to infect bacteria only and has no optimized strategies to transfer genes in mammalian cells. However, we previously reported that phage gene transfer is amenable to evolve and that one efficient strategy is to combine bacteriophage with the attributes of animal viruses. Yet, to date most progress in phage vectors has mainly been made at the genome level, which is one last step of a series of phases involved in gene transfer. Therefore, we investigated the extracellular and intracellular barriers to bacteriophage and found that one of the limitations in phage is its surface negative charge hindering phage accessibility to the negatively charged eukaryotic cell membranes. Next, we found that after internalization, the major intracellular obstacle to bacteriophage is phage sequestration in acidic endosomal vesicles, and its subsequent degradation in the lysosomal compartment. Consequently, we developed a multifunctional M13 phage that combines multiple strategies, for resolving the mammalian cell barriers, into one single particle. To improve phage accessibility to the cell surface, we generated hybrid complexes between phage and cationic polymers. Next to enhance phage escape from endosomes, we displayed endosome escape-peptides on the phage major coat protein. We showed that the multifunctional phage complex provides substantial gene expression over parental phage while retaining cell targeting and nontoxicity. Moreover, multifunctional phage complexes carrying a therapeutic gene produced greater targeted killing of cancer cells compared to phage. This new class of hybrid multifunctional platform should advance targeted gene transfer applications of phage.

Biography

Amin Hajitou obtained his BSc from the University of Fes, Morocco, then Master and PhD from the University of Liège, Belgium. His PhD involved use of retroviral vectors for oncogene transfer. Next, he enhanced his skills in vector technologies using viral vectors to systemically deliver inhibitors of tumour angiogenesis invivo. In 2002, he joined the MD-Anderson Cancer Center, Texas-USA. There, he acquired substantial expertise in phage technologies and designed new generation of hybrid phage nanoparticles for targeted systemic gene delivery. In 2007, he established his group, as a Lecturer, at Imperial College London and became Senior Lecturer in 2013.

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