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Jean Pascal Lepetit

*Universite Laval*, [alain.garnier@gch.ulaval.ca](mailto:alain.garnier@gch.ulaval.ca)

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## AN INNOVATIVE PROTEIN DELIVERY SYSTEM FOR THERAPEUTIC CELLS

Jean-Pascal Lepetit-Stoffaes, Université Laval & Feldan  
alain.garnier@gch.ulaval.ca  
Thomas Del'Guidice, Feldan,  
Joannie Roberge, Feldan  
Mario Harvey, Feldan  
Louis-Jean Bordeleau, Feldan  
Bruno Gaillet, Université Laval  
David Guay, Feldan  
Alain Garnier, Université Laval

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Cell therapy has been on the rise in recent years. It consists in the treatment of therapeutic cells to be transferred to human patients, and is applied in multiple pathologies such as hemophilia or muscular dystrophies. Several cell treatment solutions are currently developed, including the use of transcription factors or genome editing technologies. These *ex vivo* technologies often require gene transfer to express the therapeutic protein in the treated cells. The genes are delivered mainly by transfection or viral transduction, causing regulatory limitations for clinical studies.

A promising strategy is to avoid the use of nucleic acids by direct delivery of the therapeutic protein. This approach permits a transient treatment of the cells and the control of the intracellular dose of the protein. Lipids and cationic polymers offer efficient cargo delivery but present strong cell toxicity, inconsistent with human therapy. In the case of the genome editing revolution, the Cas9 system is often transferred in several plasmids, or delivered in protein with its RNA by electroporation. However, this method is afflicted by high cost, inconsistency and cell mortality. Moreover some cell lines are impervious to genome editing.

We are presently developing protein-based shuttles, designed for protein delivery in mammalian cells, specifically for cell therapy. This shuttle permits an efficient delivery of protein cargos in multiple cell lines, and is able to aim different cell compartments. Our technology has been applied for the delivery of fluorescent proteins (GFP, mCherry), antibodies, a transcription factor, and also the Cas9 nuclease. Our technology has a low cytotoxicity and the naturally degradable shuttle offers a transient and controlled delivery. The absence of gene transfer makes it suitable with safety regulation. Feldan Shuttle is a high potential method which can be a strong contender for cell therapy applications, bringing transcription factors development and genome editing technologies to clinical studies.