# High-throughput microfluidic device for the analysis at single cell level

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The promising of gene delivery as innovative therapeutic tool relies on the development of DNA-carrying vehicles featuring a compromise to achieve useful gene transfer efficiency while maintaining low toxicity. While non-viral gene vectors offers great potentialities in this direction, their low transfection efficacy leads to the necessity of further optimizations. Aiming at overcoming the limitation of traditional macroscale approaches, mainly consisting in time-consuming and simplified models, a microfluidic strategy was developed for transfection studies on single cells in a high-throughput and deterministic fashion. A single cell trapping mechanism was implemented based on dynamic variation of fluidic resistances. At this purpose, a round-shaped culture chamber (Φ=250μm, h=25μm) was conceived presenting two connections with a main fluidic path: (i) an upper wide opening, and (ii) a bottom trapping junction which modulates the hydraulic resistance. Several layouts of the chamber were designed and computationally validated for the optimization of the single cell trapping efficacy. The optimized chamber layouts were integrated in a polydimethylsiloxane (PDMS) microfluidic platform presenting two main functionalities: (i) 288 single chambers for trapping single cells (ii) a chaotic mixer serial dilution generator for delivering both soluble factors and non-diffusive molecules (i.e. non-viral gene vectors) under spatio-temporally controlled chemical patterns. The devices were experimentally validated and allowed for trapping individual human glioblastoma-astrocytoma epithelial-like cells (U87-MG). Seeded cells were then cultured within the device and preliminary transfection experiments were performed using 25kDa linear polyethylenimine confirming the potentiality of the proposed platform for optimizing gene delivery and cell transfection protocols.