

## AMPHIPHILIC DENDRIMER/DNA SELF-ASSEMBLIES FOR CELL TRANSFECTION. A SCANNING PROBE MICROSCOPY STUDY.

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**INTRODUCTION:** Amphiphilic dendrimers were designed to combine a high charge density and spontaneous self-assembly properties to condense DNA [1-2]. After promising biological transfection results, Scanning Probe Microscopy gives insight into structure-activity relationships.

**METHODS:** The amphiphilic vectors **1-4** (Fig. 1) have been synthesized. The two parts, lipophilic and hydrophilic dendrons, are connected to a rigid scaffold. After extended biological investigations, the study on surfaces has been focused by using AFM in tapping mode on freshly cleaved mica surfaces with drop cast of dendrimer, plasmid and a mixture of dendrimer/plasmid depending of the charge excess (CE).

To a better understanding of the amphiphilic compounds behavior, measurements were done at the air-water interface by recording the isotherms and exploiting Brewster Angle Microscopy, X-Ray reflectivity and tapping mode AFM on Langmuir Blodgett films.

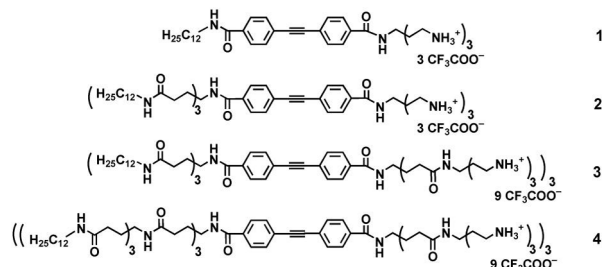


Fig. 1: A novel class of amphiphilic dendrimers.

**RESULTS & DISCUSSION:** Compounds **2** and **3** were found to be highly efficient transfection agents (Fig. 2). The study purchased in AFM showed (Fig. 3) complexation properties of the dendrimer **2** with the same plasmid used for the cell transfection.

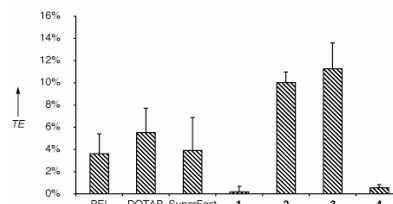


Fig. 2: Gene transfection efficiency study

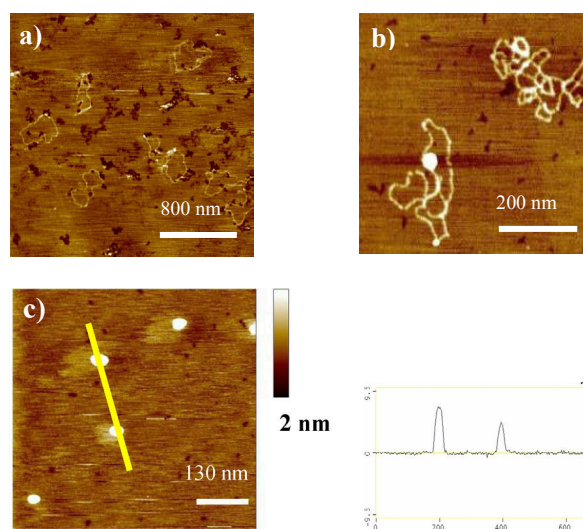


Fig. 3: Tapping mode AFM images on freshly cleaved mica: a) Plasmid deposition. b) Plasmid deposition followed by dendrimer **2** drop-cast showed 'prior' coiling state. c) Plasmids and **2** were mixed prior to deposition, showing polyplexes formation.

**CONCLUSIONS:** Our approach allows to tune the complexation properties of amphiphilic compounds and we will use AFM as a predictive tool for their transfection properties [3].

**REFERENCES:** <sup>1</sup>J-P. Behr, *Bioconjugate Chem.*, **1994**, *5*, 382-389. <sup>2</sup>D. Joester *et al.*, *Angew. Chem. Int. Ed.*, **2003**, *42*, 1486-1490. <sup>3</sup>H. G. Hansma *et al.*, *Nucleic Acids Research*, **1998**, *26*, 2481-2487.