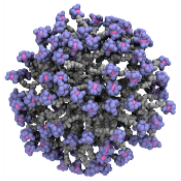
cost

EUROPEAN COOPERATION
IN SCIENCE & TECHNOLOGY



COST ACTION CA 17140

NANO2CLINIC

CANCER NANOMEDICINE - FROM THE BENCH TO THE BEDSIDE

UNIVERSITÀ DEGLI STUDI DI TRIESTE

STSM - September 2021

Pr. Sabrina PRICL

Cancer Nanomedicine via Dendrimer Nanocarriers

Aura TINTARU

Aix*Marseille université

CINaM

Centre Interdisciplinaire de Nanoscience de Marseille – UMR 7325

5 Research Departments : 120 permanents; 60 PhD and post-docs
Aix-Marseille Université, Campus Luminy

February 23rd, 2023

Overview

Main research project: DENDRIMERS

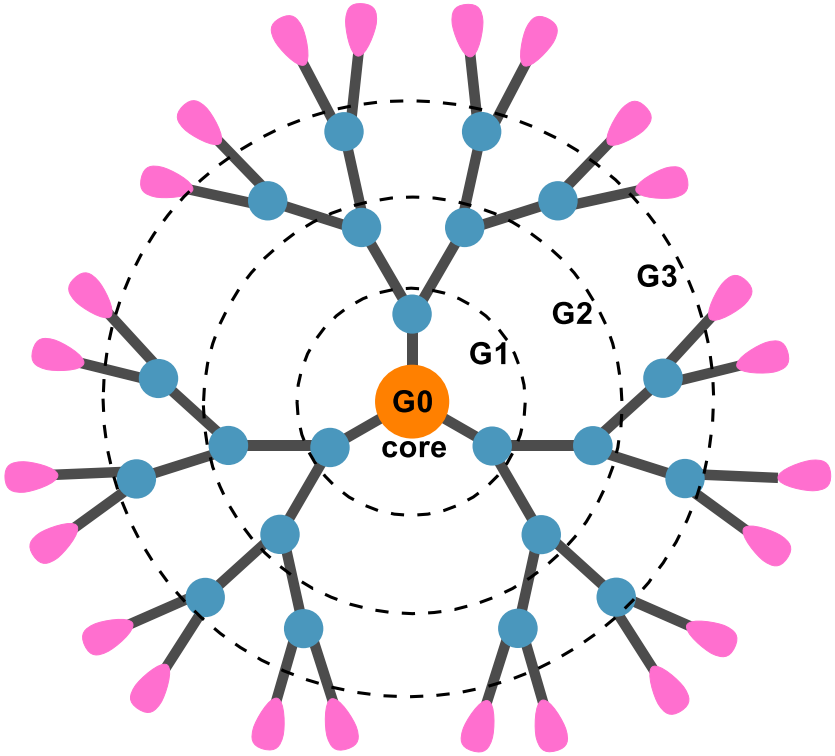
Complex molecules

↓

Vectorisation agents

↓

Original analytical approaches adapted to each specific topic



Combinative approach: NMR-MS

J.M. Fréchet and D. A. Tomalia : Dendrimers and Other Dendritic Systems (2001) John Wiley & Sons
G. R. Newcome et al: Dendrimers and Dendrons (2002) John Wiley & Sons

Overview

Nano2Clinic
CA17140

Main research project: DENDRIMERS

Complex molecules

↓

Vectorisation agents

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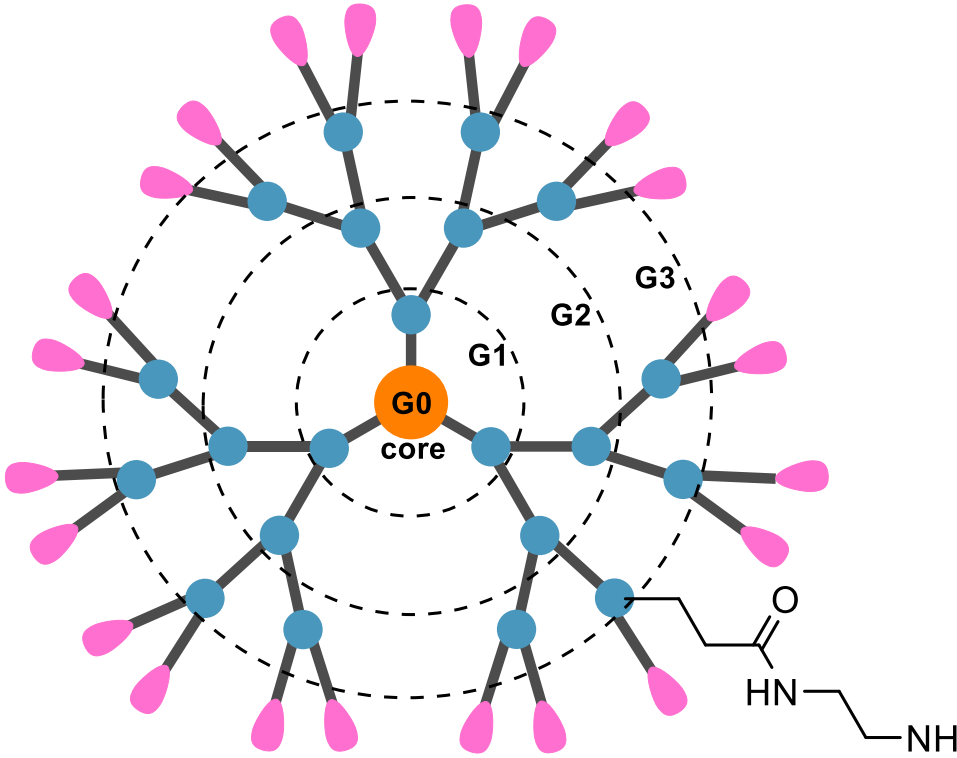
Original analytical approaches adapted to each specific topic



PAMAM – poly(amido)amine

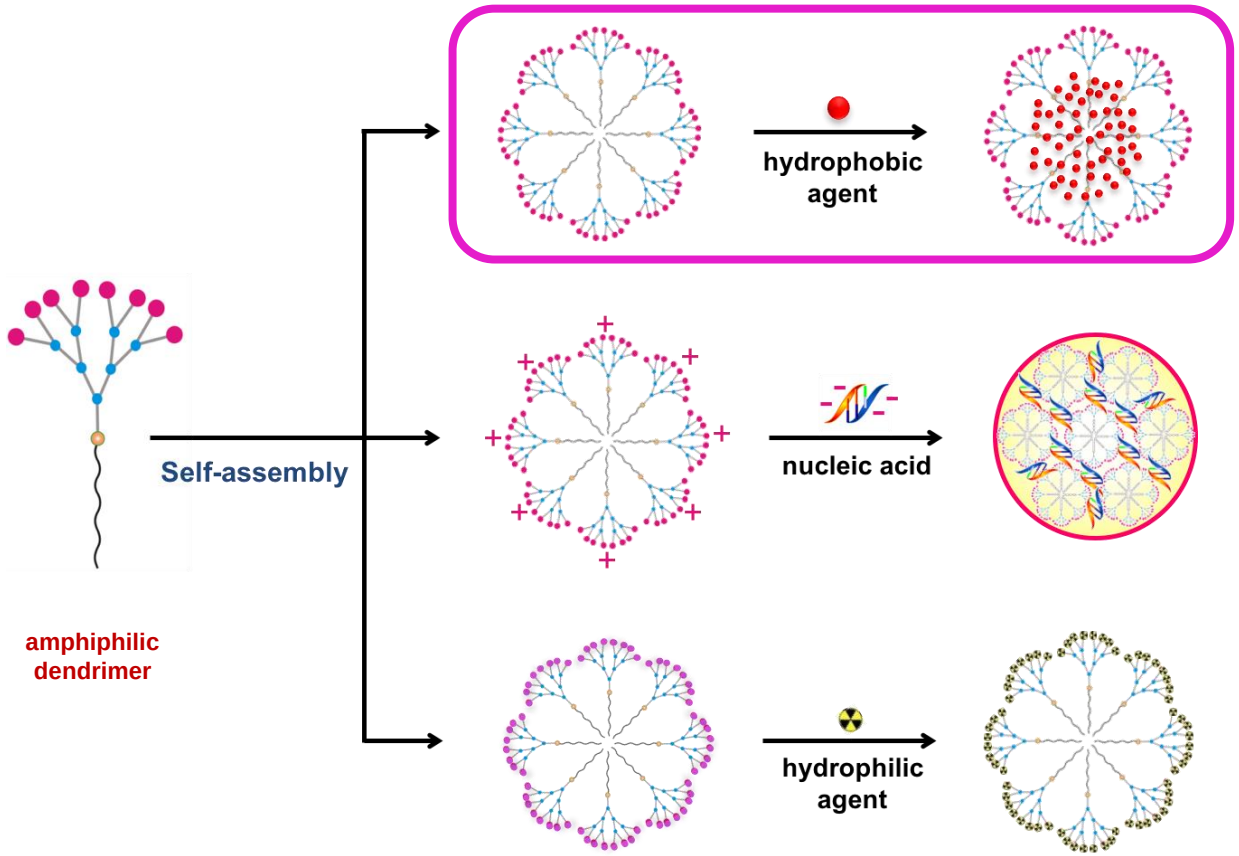
Combinative approach: NMR-MS

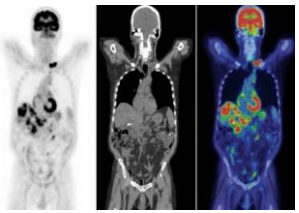
Main goal: Accurate characterization

February 23rd, 2023

Overview

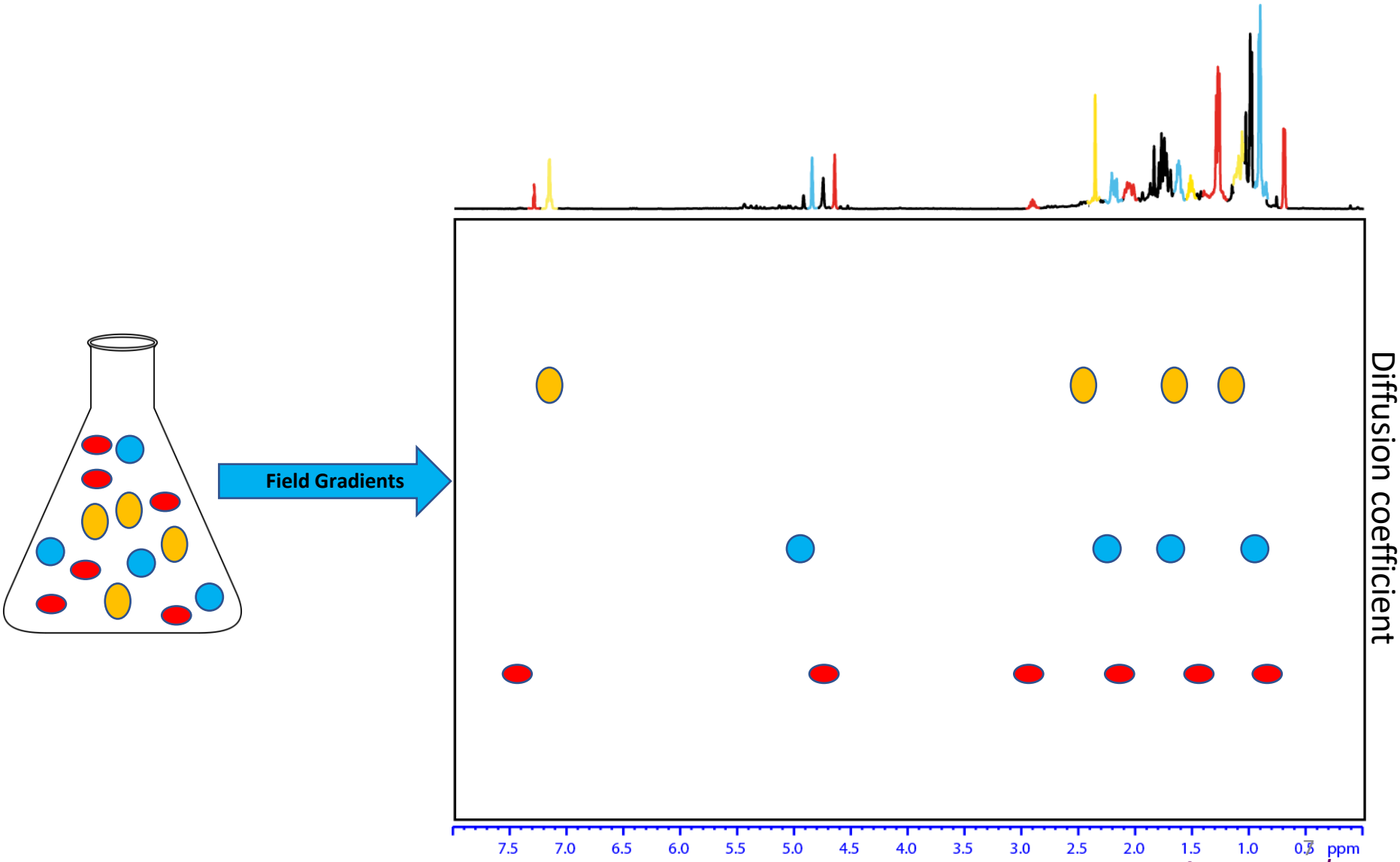
Amphiphilic Dendrimers



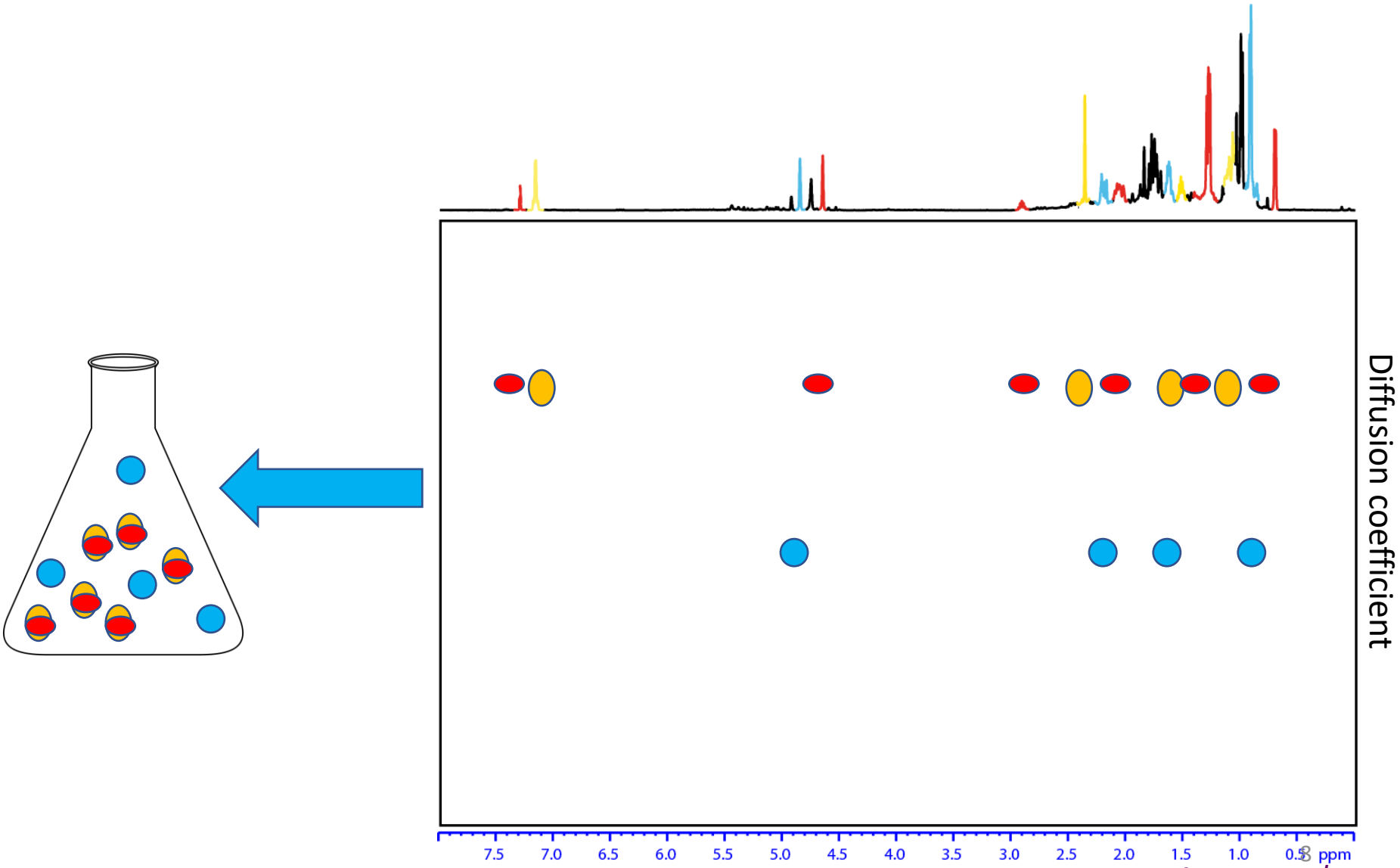


Lyu et al, *Acc Chem Res* **2020**,*53*, 2936

Diffusion NMR



Diffusion NMR



Contexte

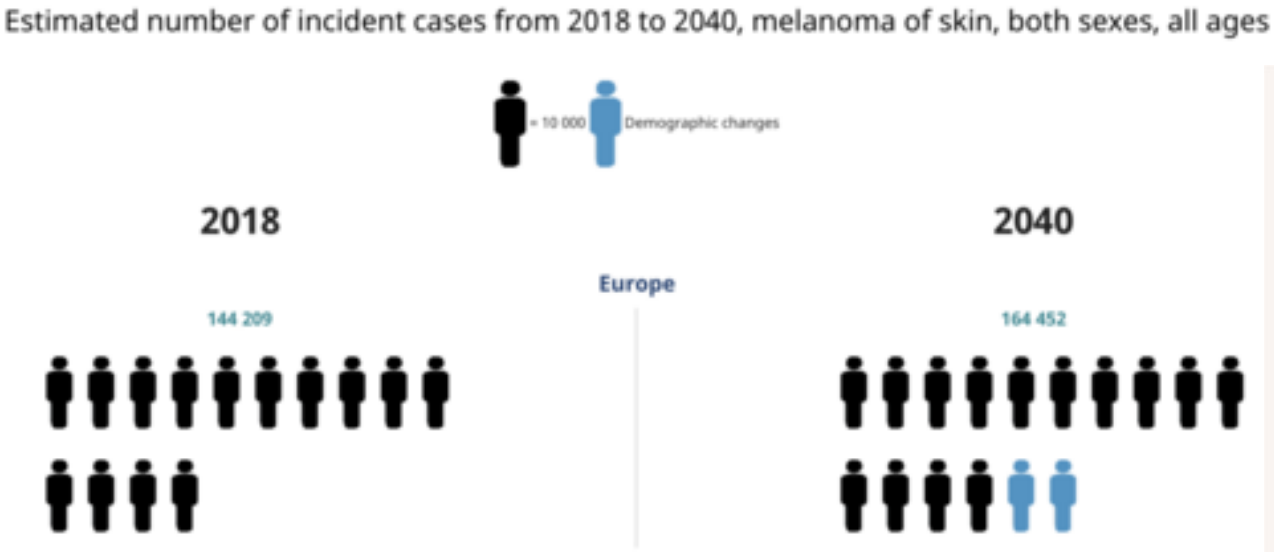
Melanoma in brief

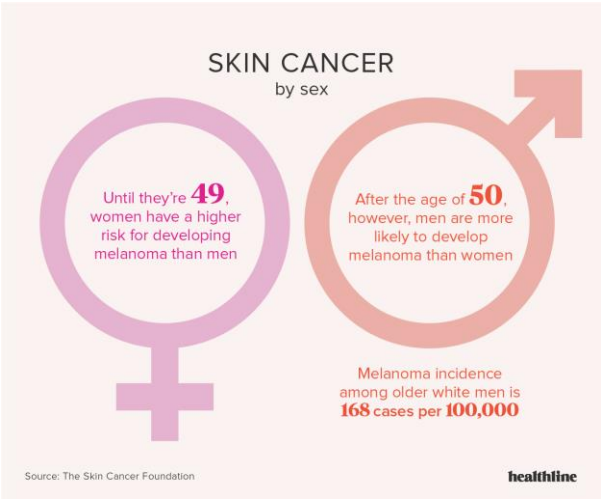
- Cancer starting from pigment-producing cells, mostly but not only in the skin
- Survival very dependent on stage: Detected early, high chances of survival by surgery alone (95% cured). Detected late, fatal prognosis (average survival 6- 9 months without new medicines)
- 144 000 new cases / year in Europe
- 27 000 deaths / year in Europe
- Traditional therapies alone (surgery, radiotherapy, chemotherapy) not effective once the disease has spread
- 10 new therapies plus combinations approved since 2011
- Patient highly dependent on innovative approaches to development of and access to new therapies

Globocan 2018; Gershenwald 2017

Contexte

Melanoma in facts





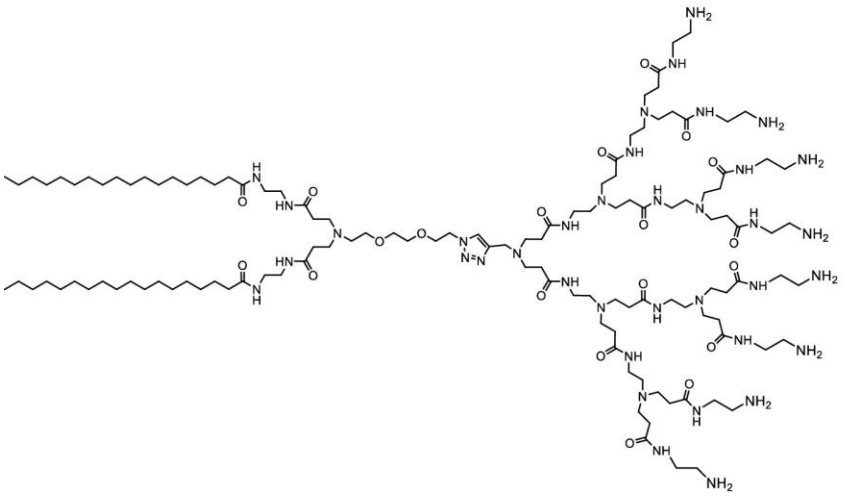
Main limitations of today therapies (based on BRAF inhibitors)

- side effects
- oral administration less efficient than intravenous

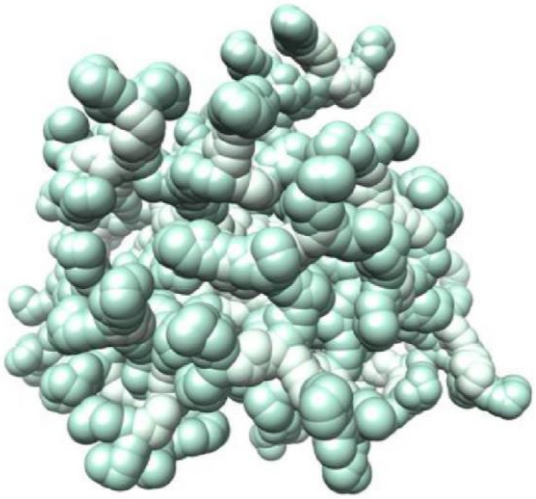
} Proof of concept :
BRAFinhib delivery by nanocarrier

Liu X et al, *Angew Chem Int*, **2014**, *Acc Chem Res* **2020**,*53*, 11822

Nanocarrier Formation



Self-assembly



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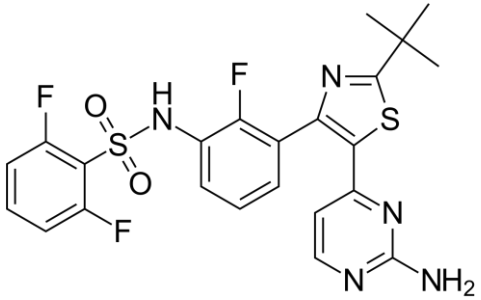
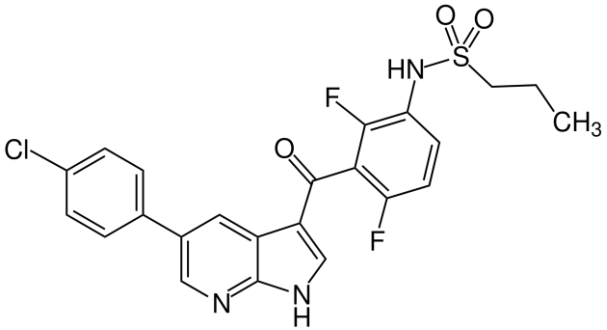
Drug Loading



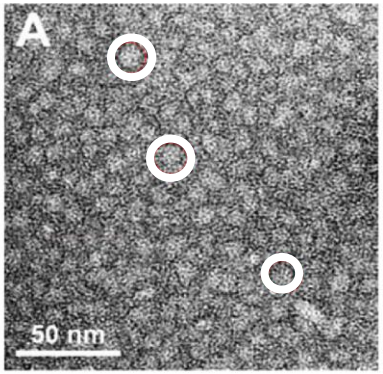
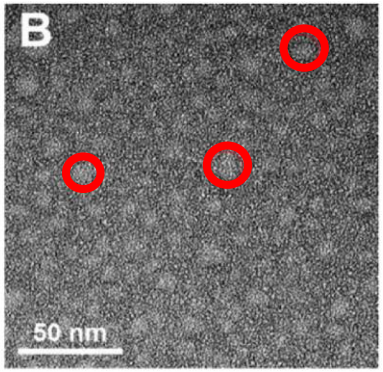
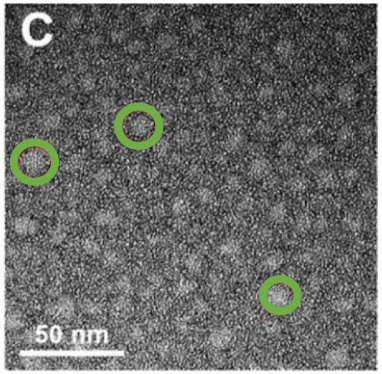
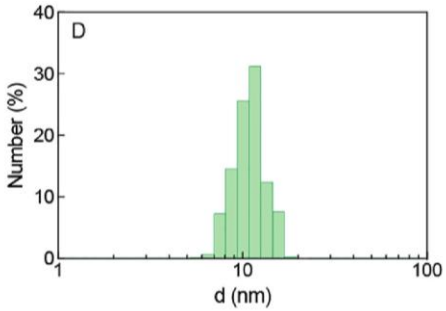
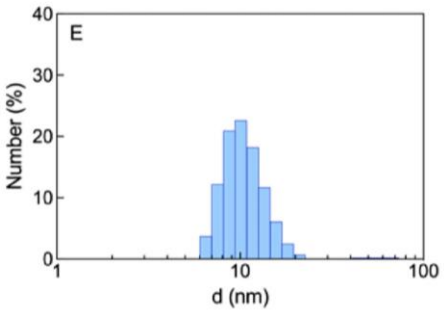
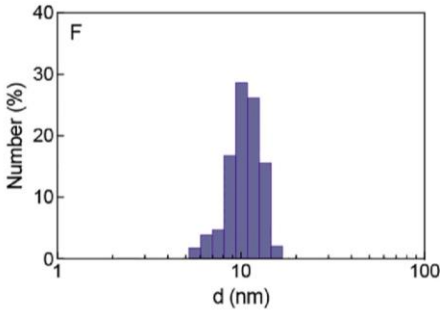
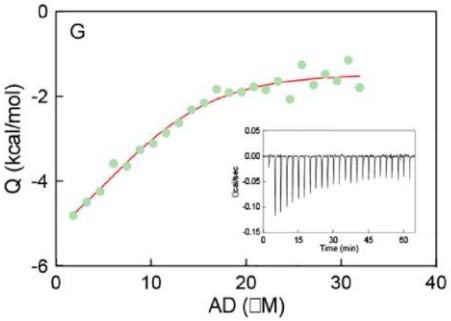
Vemurafenib



Dabrafenib

Liu X et al, *Angew Chem Int*, **2014**, *Acc Chem Res* **2020**,*53*, 11822

Nanocarrier Observation

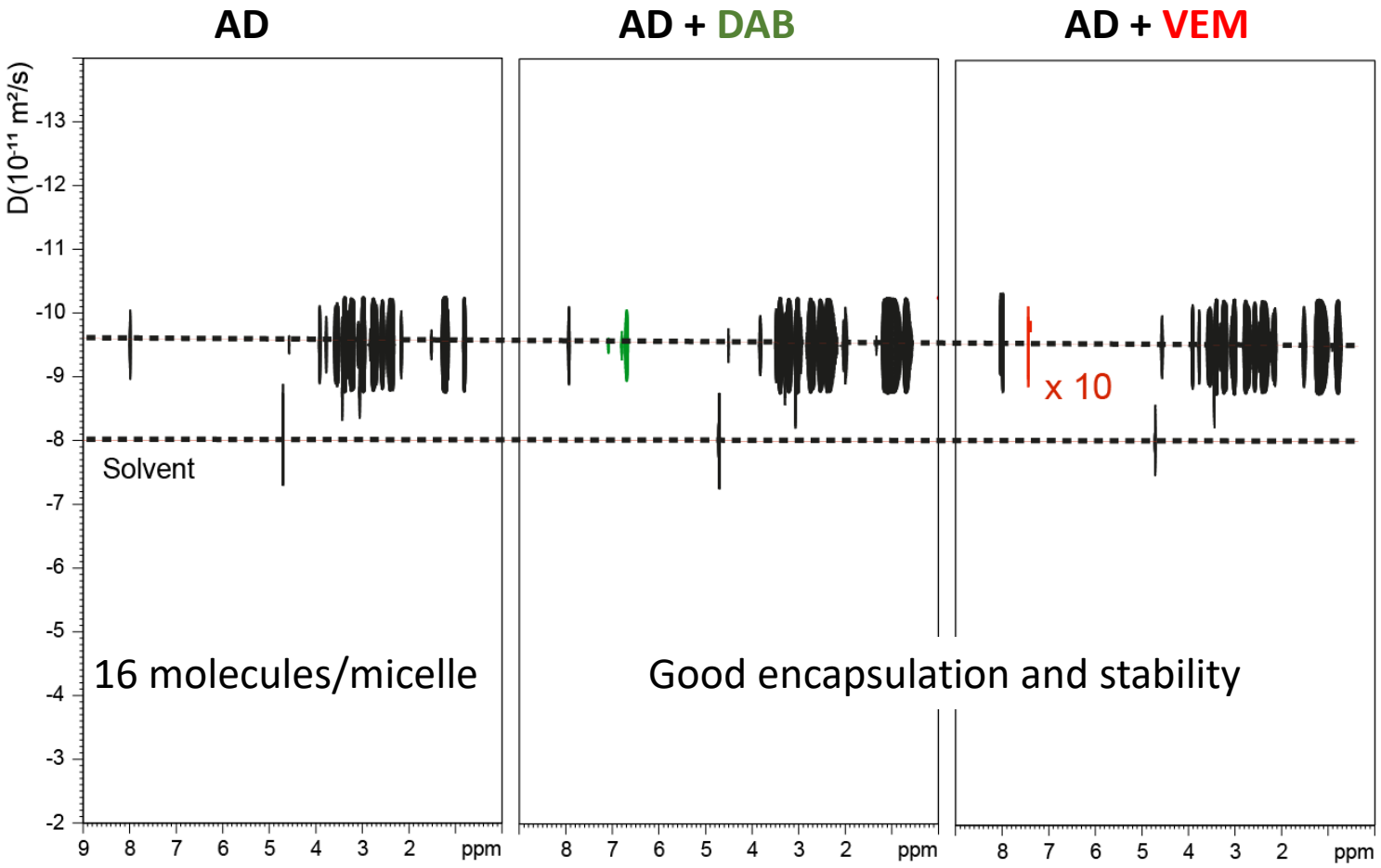
	AD	AD + DAB	AD + VEM
TEM			
DLS			
ITC			

~4nm

Russi M et al, *Eur J Pharmac Sci*, **2022**, 180, 106311

Nanocarrier Characterization

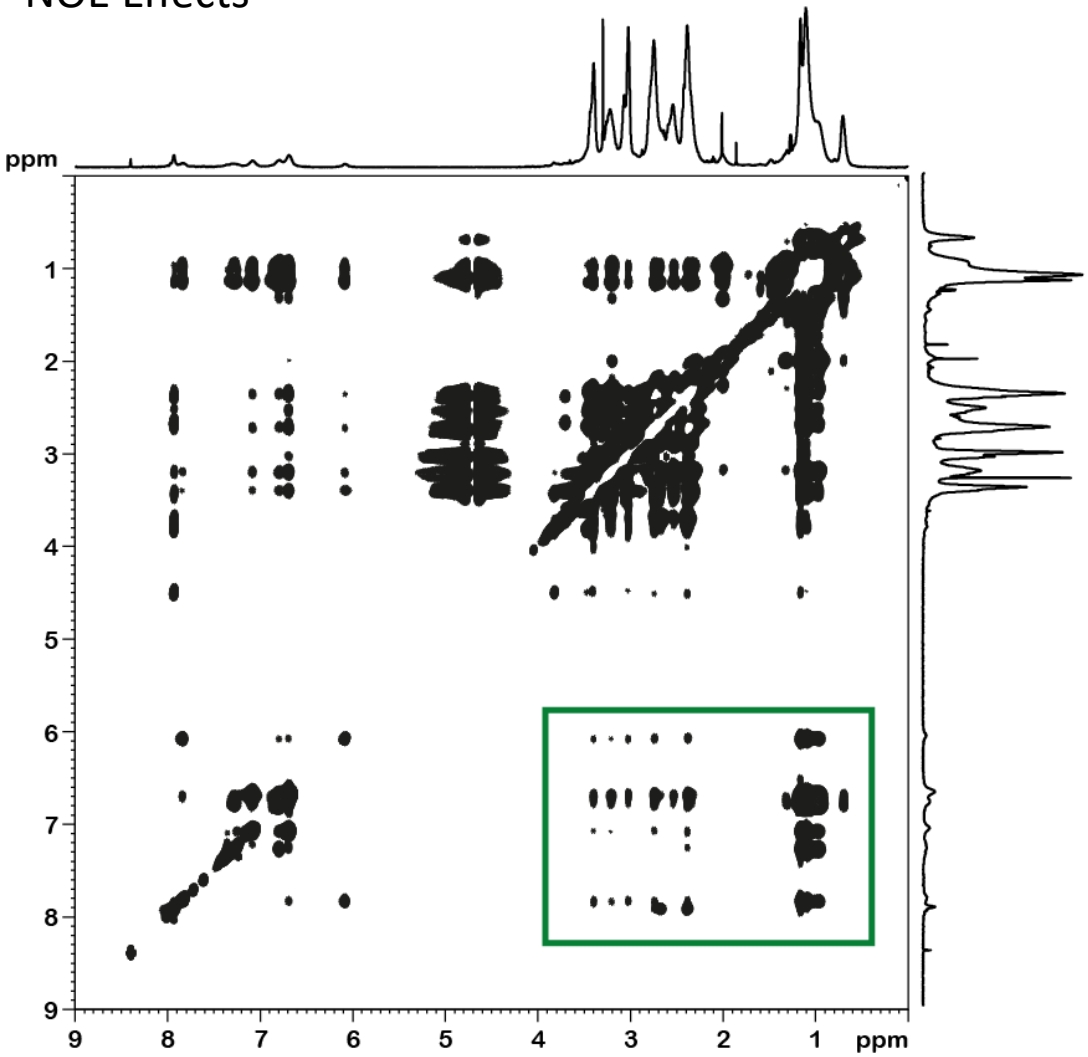
Diffusion NMR (DOSY)



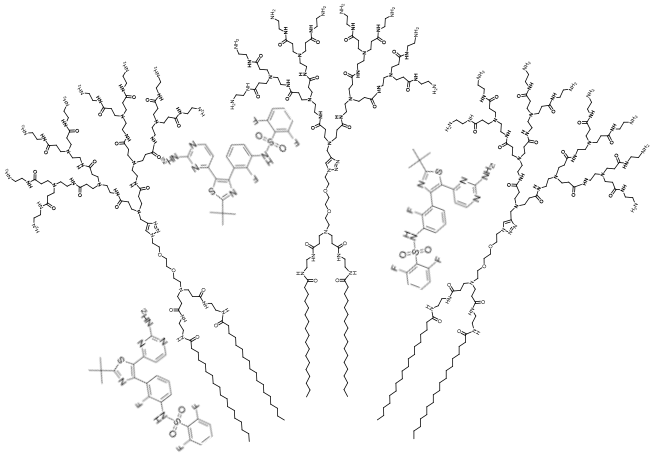
Russi M et al, *Eur J Pharmac Sci*, **2022**, 180, 106311

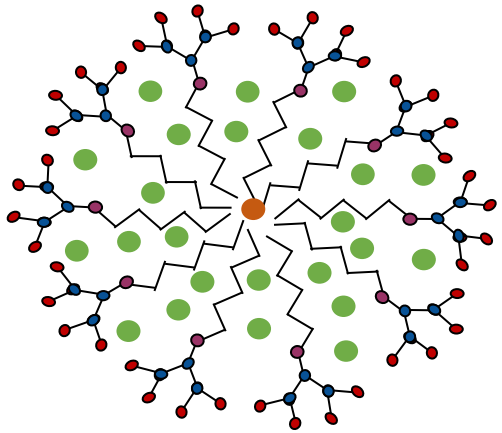
Nanocarrier Characterization

NOE Effects



AD/Dabrafenib



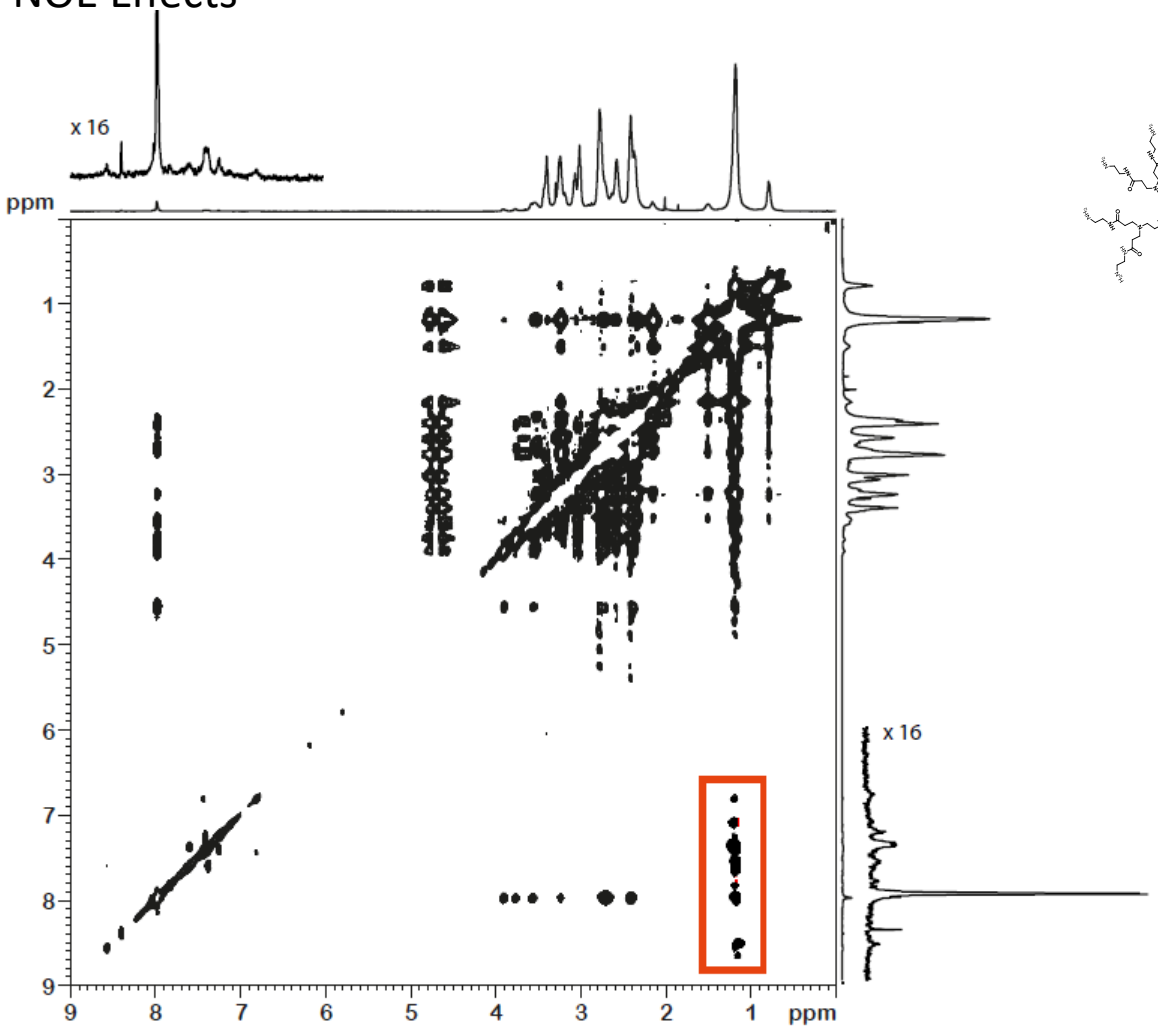


DAB interacts with the hydrophobic & hydrophilic part

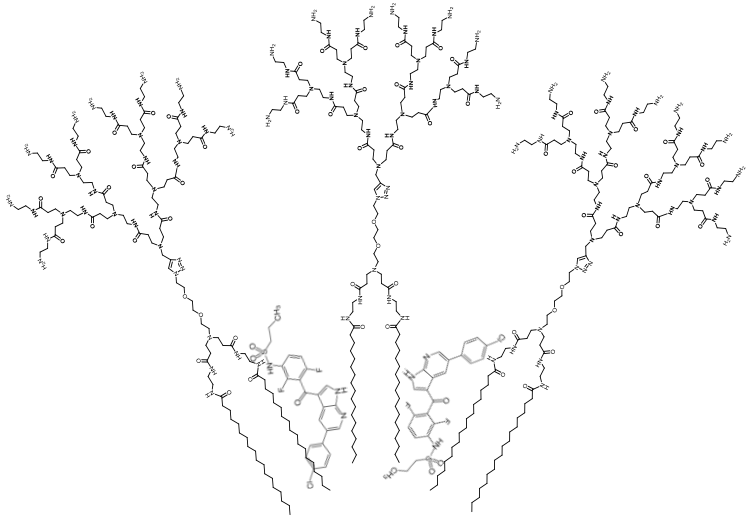
Russi M et al, *Eur J Pharmac Sci*, **2022**, 180, 106311

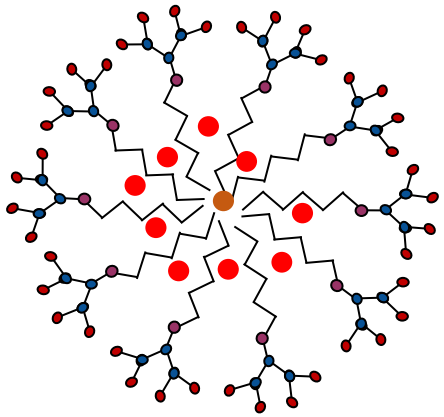
Nanocarrier Characterization

NOE Effects



AD/Vemurafenib



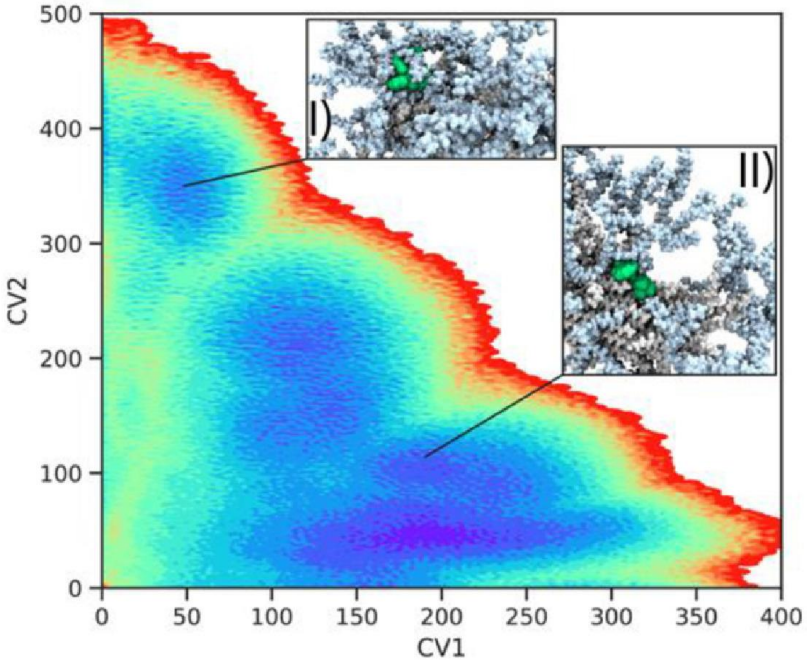


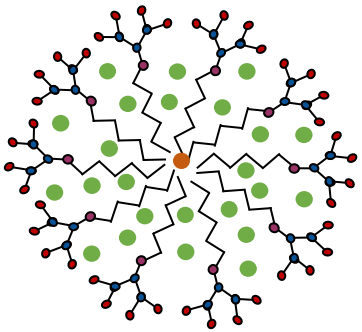
VEM interacts with the hydrophobic part

Russi M et al, *Eur J Pharmac Sci*, **2022**, 180, 106311

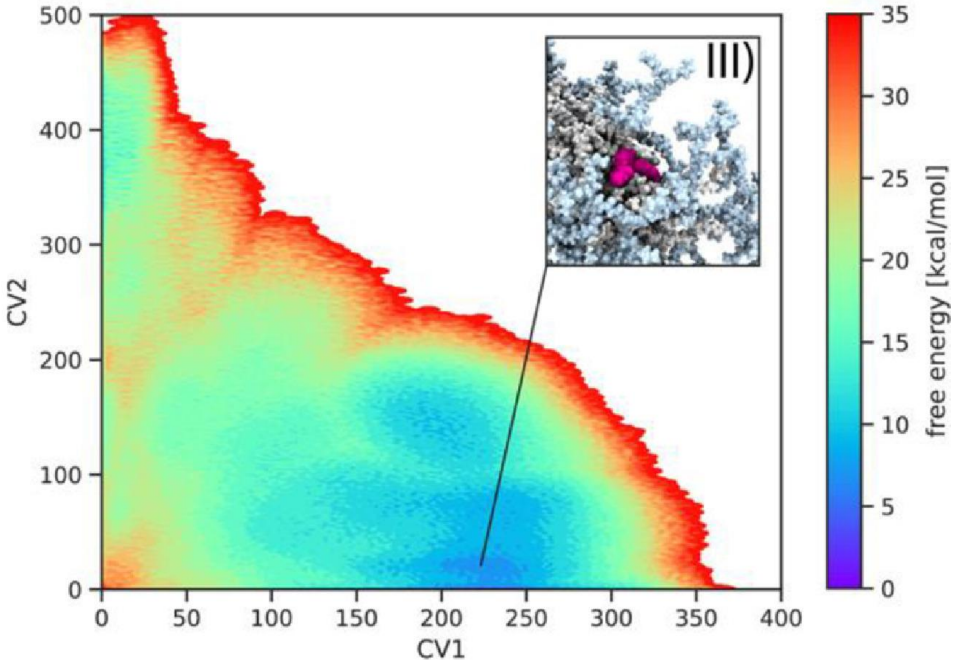
Nanocarrier Characterization

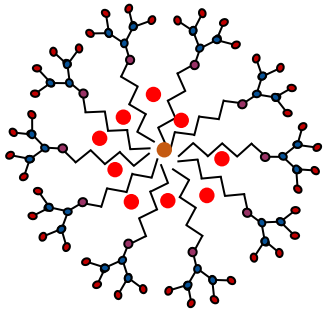
Dabrafenib





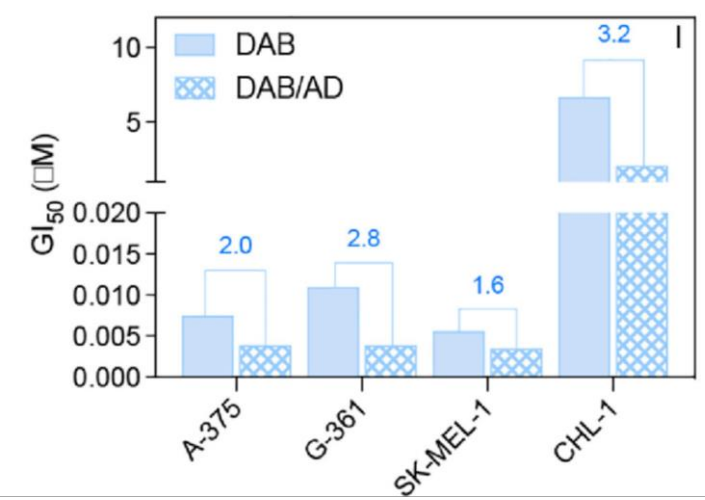
Vemurafenib

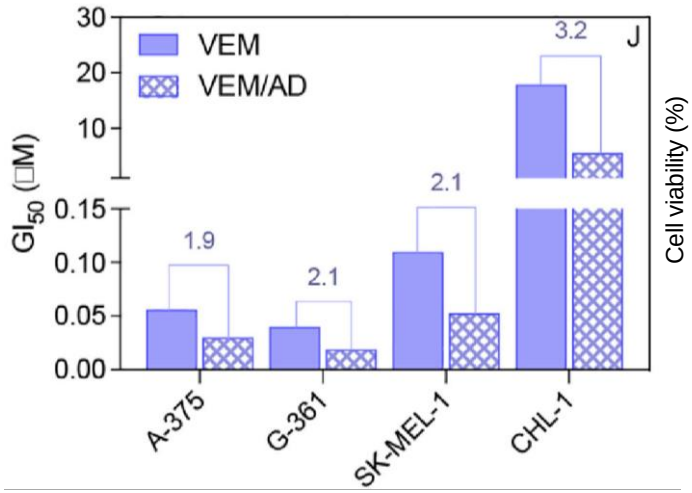


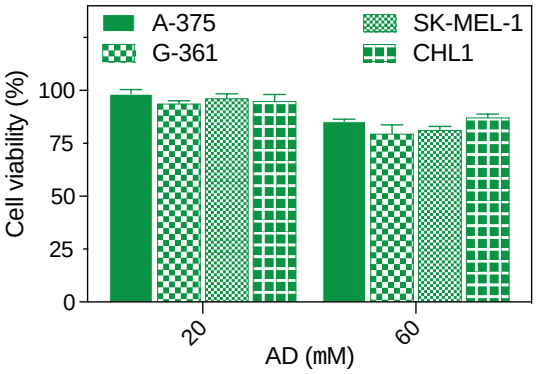


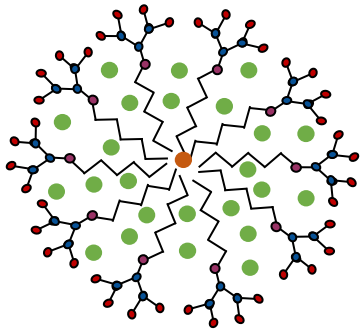
In vitro Anticancer Activity Assays

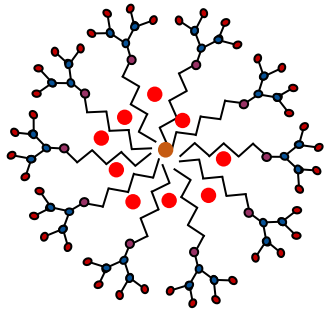
4 human malignant melanoma cells

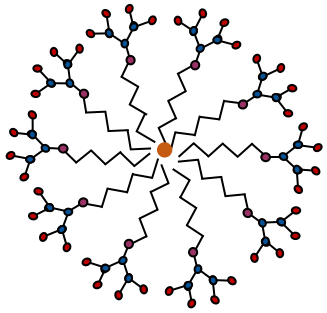












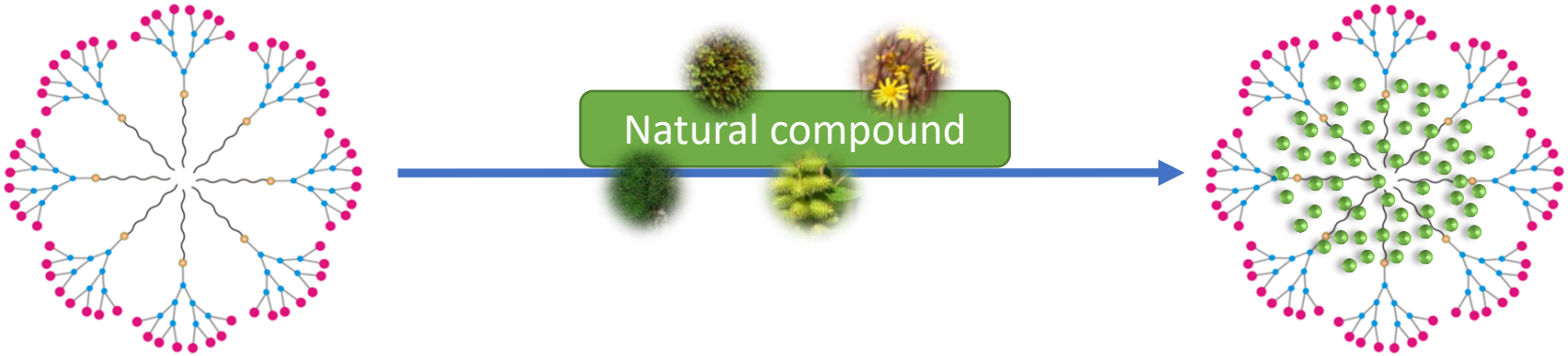
Conclusion

- **Successful formulation of drug loaded nanomicelles using amphiphilic dendrimers (AD)**
- **Stability of the DAB/AD and VEM/AD carriers**
- **Good anticancer activity**
- **NM/drug: Promising improvement compared with free drug**

Perspective

Nano2Clinic
CA17140

Nanocarriers for « natural » drugs delivery



Controllable structure

Stable formulation

High drug payload

Low toxicity

Stabilisation

Controlled targeting

Novel and powerful dendrimer nanocarriers

February 23rd, 2023

Why natural products?

- The simplest definition for a **natural product** is a **small molecule** that is produced by a **biological source**.

- **One third** of the new reported molecules are obtained from **plants**

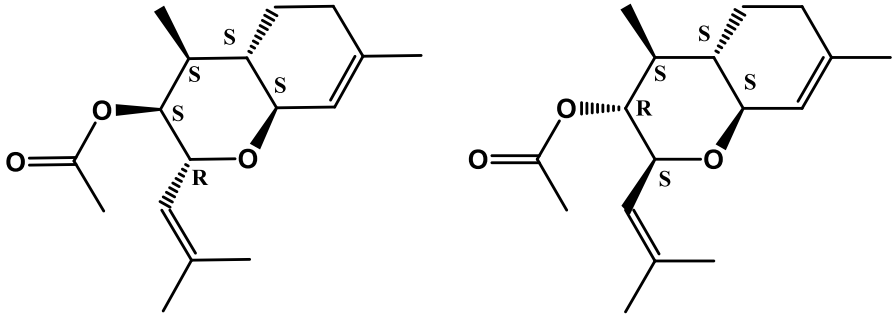
- A full **40 percent** of the drugs behind the pharmacist's counter in the Western world are derived from plants that people have used for centuries

- **Cosmetic industry** : The Natural and Organic Cosmetics market in the U.S. is estimated at **5 Billion US dollars** in **2020**

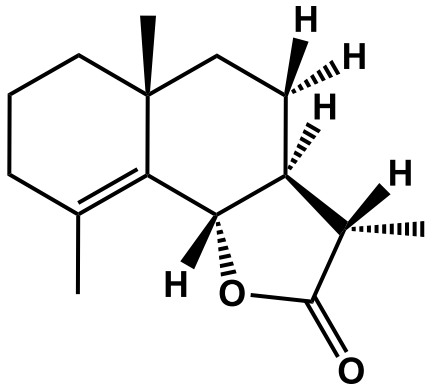
- **Corsica** island: aprox. **3000** species (> 2500 indigens)

High POTENTIAL for new pharmaceutics development!!

Senecio transiens



Frullania tamarisci



High POTENTIAL for new pharmaceutics development!!

STSM « Results »

- 1 published publication
- 2 publications to be submitted soon
- 1 project submitted for ANR funding request
- 1 fruitful collaboration

Acknowledgments

Sabrina PRICL

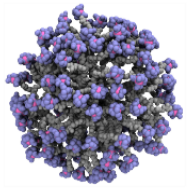
Erik Laurini

Domenico MARSON

Maria RUSSI

Fulvia FELLUGA

Ling PENG's Group



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