Catalytic polymeric micelles

Meeting 1
Eindhoven, 26th March 2019

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Tel Aviv University

Innovative Training Networks (ITN) – Marie Skłodowska-Curie Actions
H2020-MSCA-ITN-2017 (THERACAT-765497)

Institution description

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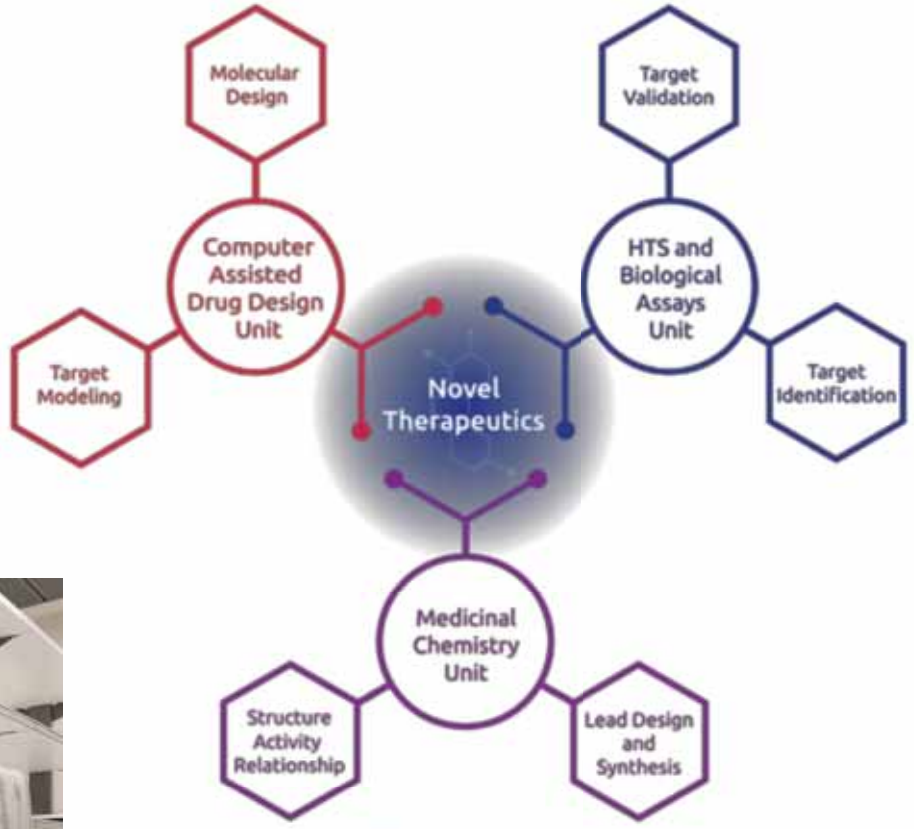
The BLAVATNIK CENTER for

Drug Discovery



The lab: polymer synthesis and characterization

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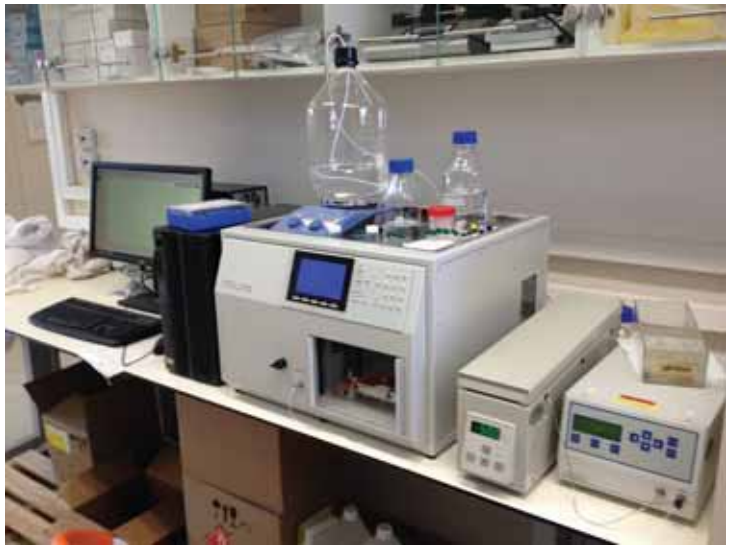
Chemistry lab

Schlenk lines

Preparative LC

GPC (IR+PDA)



HPLC (PDA)

Microwave reactor

The lab: characterizing self-assembly

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DLS

Automated sample preparation

Fluorimeter (temp controller+multi-cell holder)

Departmental facilities

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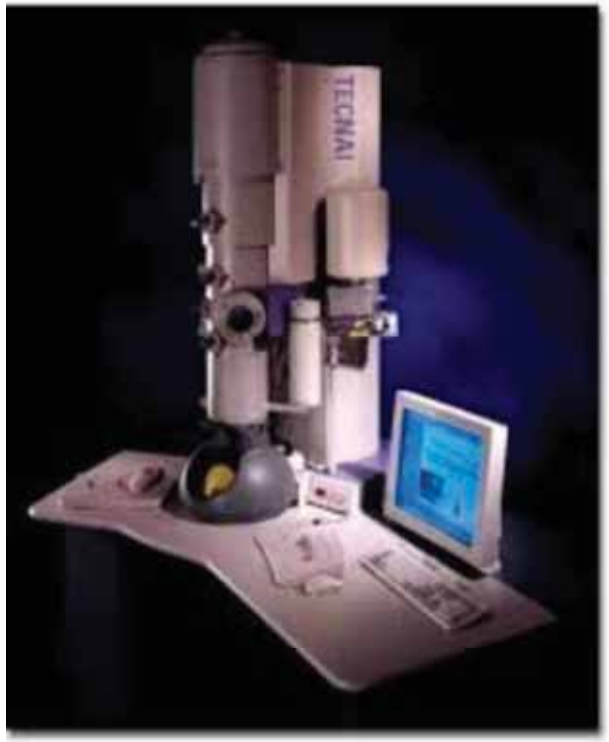
NMR

MALDI-TOF

TEM (@ TAU Nano Center)



Acknowledgments

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RAG@TAU
Assaf Harnoy
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Lihi Ozery
Shahar Tevet
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Shreyas Wagle
Daniel Peretz

SAXS
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MRI
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Biology
Prof. Ronit Satchi-Fainaro

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Yael Cohen

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TEM Dr. Einat Tirosh, Uri Hananel

Microscopy Prof. Yuval Ebenstein

Spectroscopy Dr. Tal Schwartz

SUPSI Switzerland Dr. Giovanni M. Pavan
IBEC/TUE Dr. Lorenzo Albertazzi, Natalia Feiner

European Training Network
THERACAT

ISRAEL SCIENCE FOUNDATION

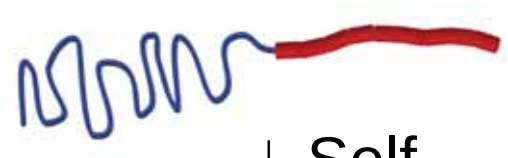
BLAVATNIK CENTER
for Drug Discovery

Tel Aviv University Center for
Nanoscience & Nanotechnology
Powering Innovation

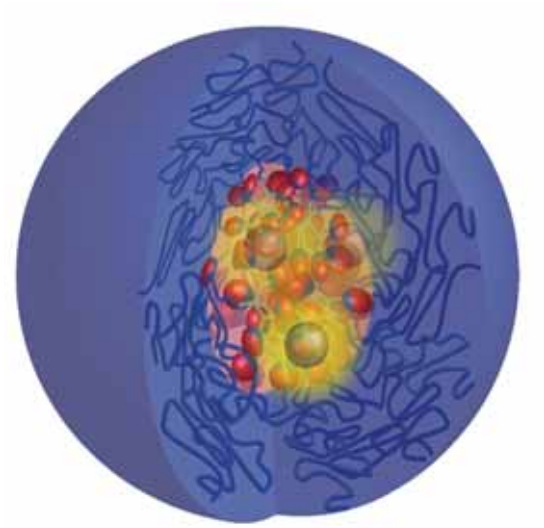
ADAMA

Using polymeric assemblies as nanocarriers

Blue = hydrophilic
Red = hydrophobic



Self assembly



Common concerns about small drug molecules:

- Poor solubility
- Get cleared quickly
- Degradation
- Non-specific

Benefits of delivery platforms:

- Improved solubility
- Long circulation times
- Protect drugs from degradation
- Can be targeted

Delivery platforms require selective release mechanisms

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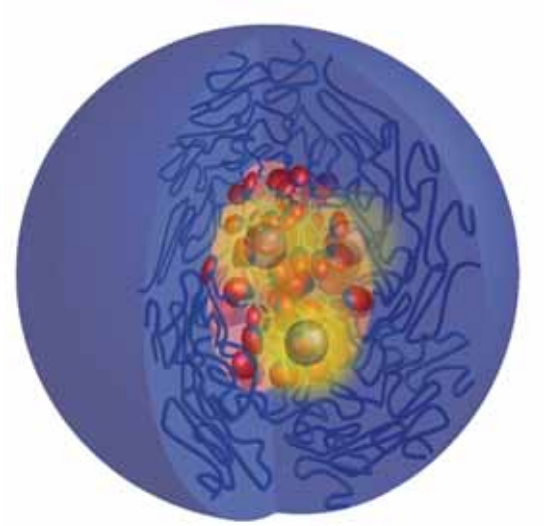
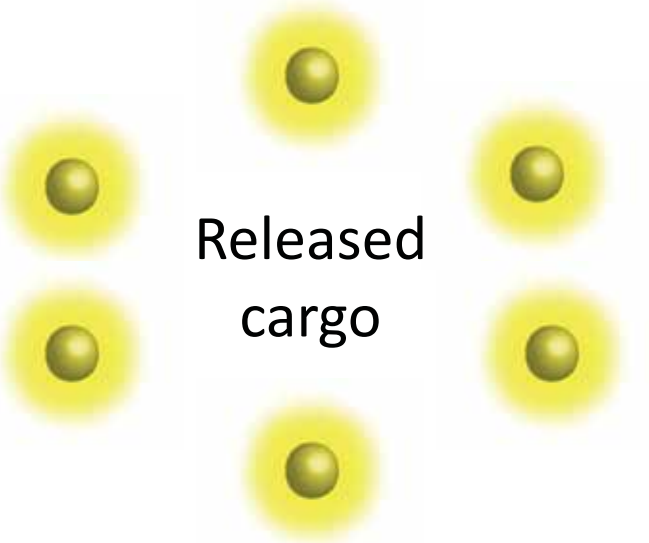
Blue = hydrophilic
Red = hydrophobic

Self assembly



Release mechanism



Structural change

hydrophilic-hydrophilic

Can enzymes access and degrade the hydrophobic blocks?

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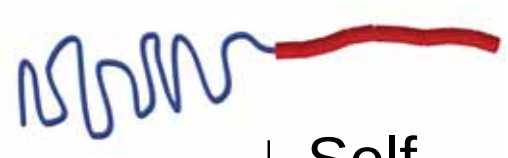
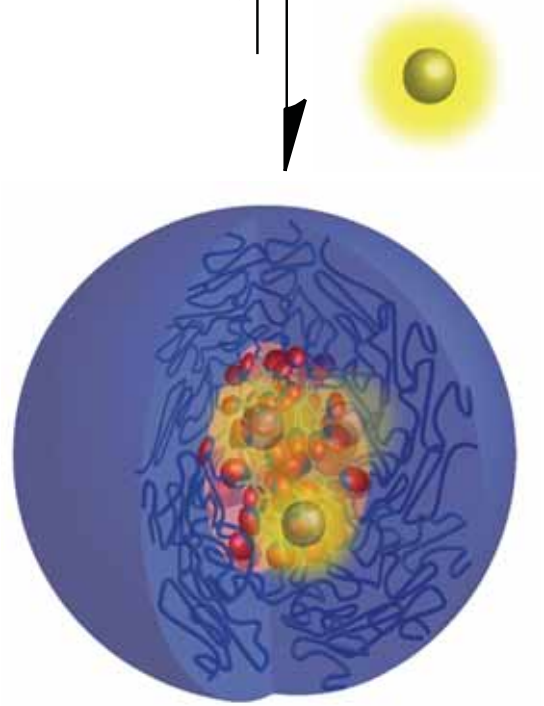
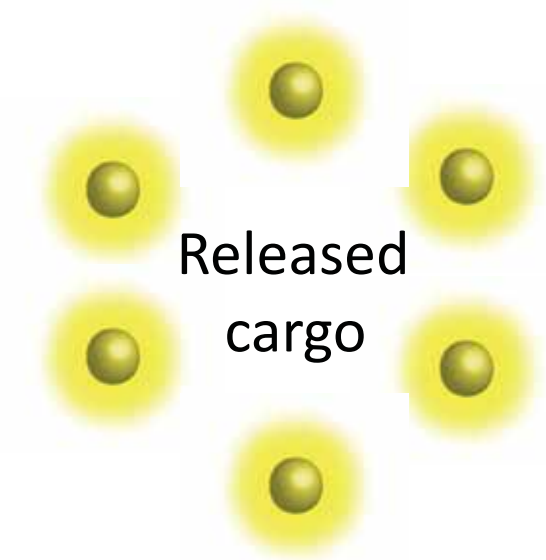
Blue = hydrophilic
Red = hydrophobic

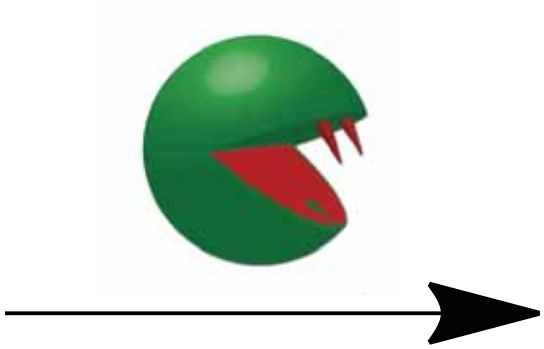


Self assembly



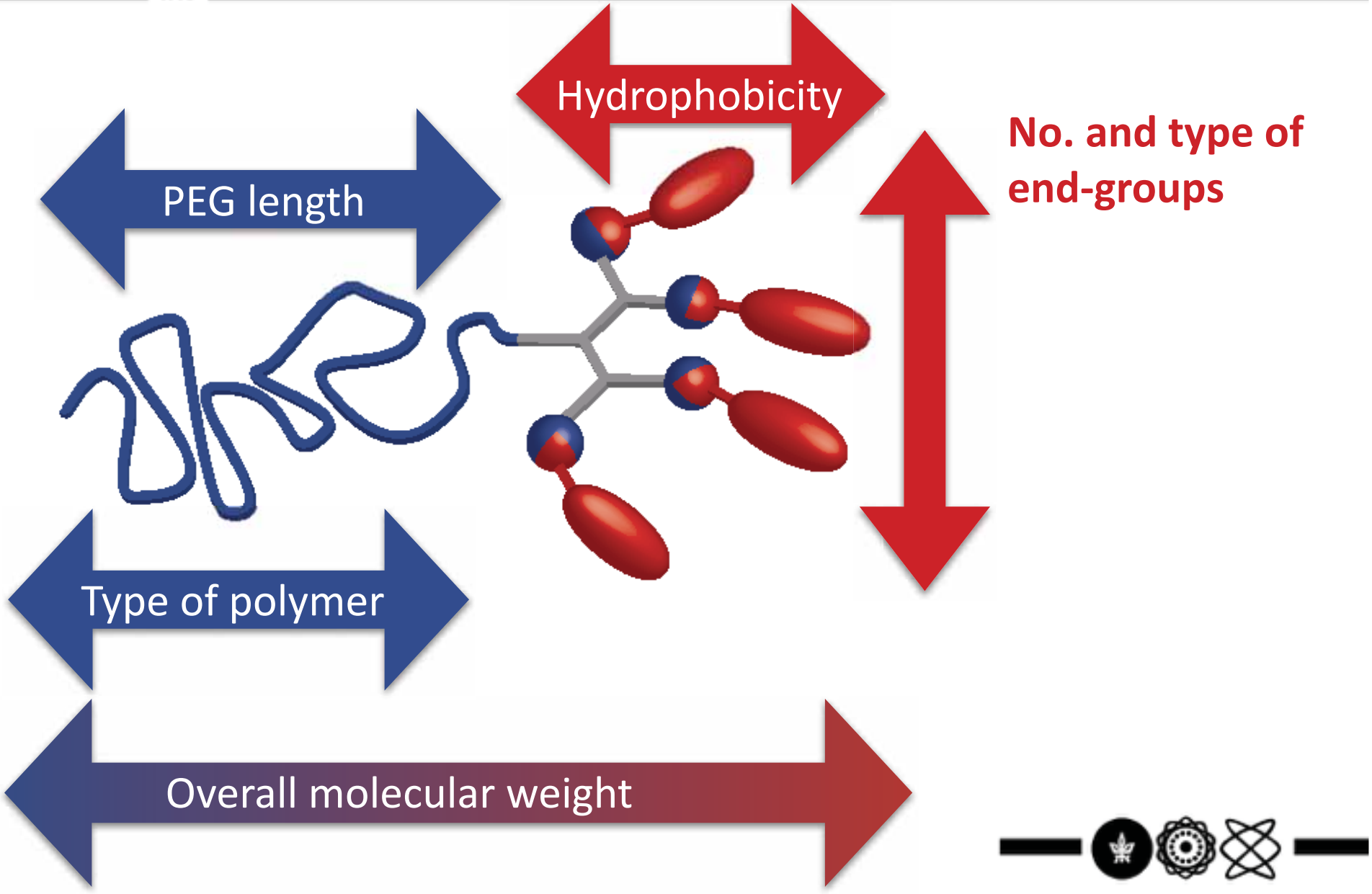
- High Selectivity
- Catalytic capabilities
- Naturally present in the body
- **Often over-expressed in diseased tissues**





hydrophilic-hydrophilic

Tuning amphiphilicity with high molecular precision



Tuning amphiphilicity with high molecular precision

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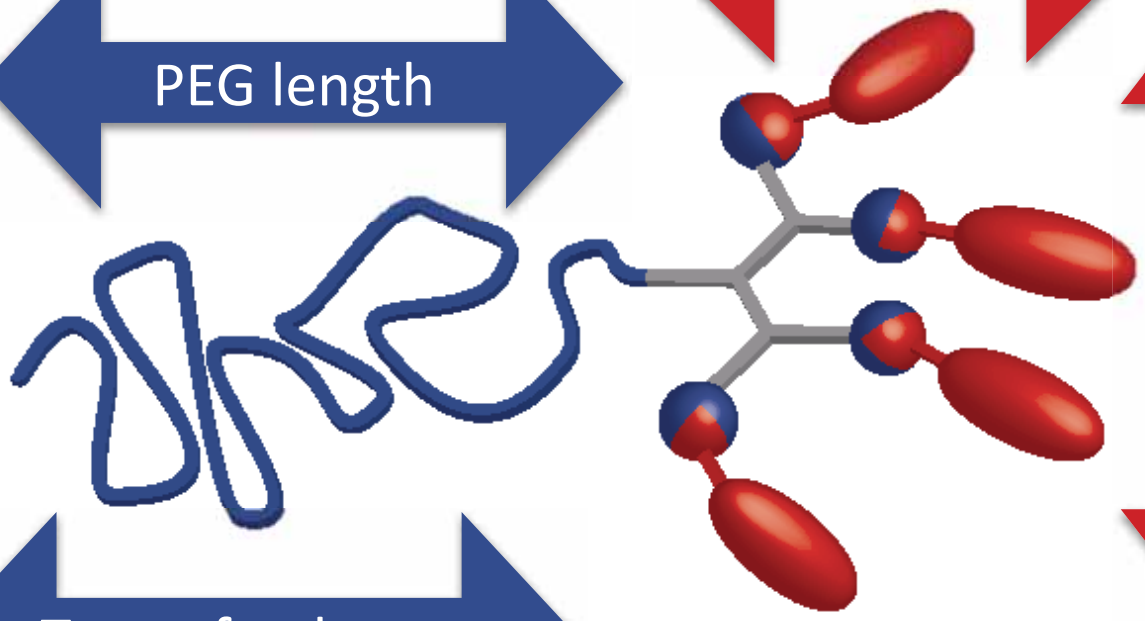
Harnoy et al. *JACS* **2014**

Hydrophobicity

PEG length



No. and type of end-groups

Rosenbaum et al. *JACS* **2015**

Harnoy & Slor et al. *OBC* **2016**

Harnoy et al. Biomacromolecules **2017**

Segal et al. *JACS* **2017**

Harnoy et al. Synlett **2018**

Type of polymer

Slor et al. *In preparation*

Slor et al. *ChemComm* **2018**

Overall molecular weight

Rosenbaum et al. *Biomacromolecules* **2017**

Labeled polymeric assemblies designed to self-report their activation

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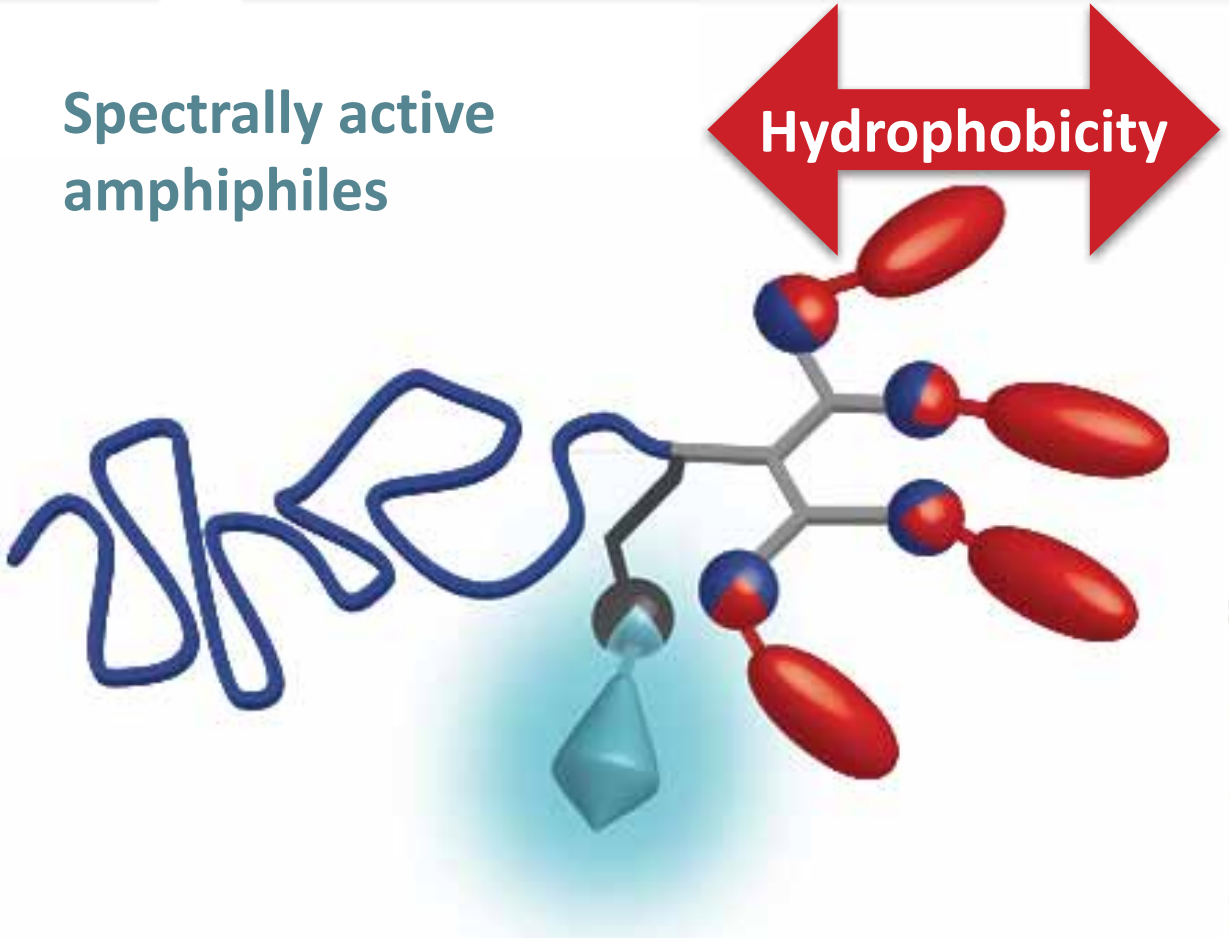
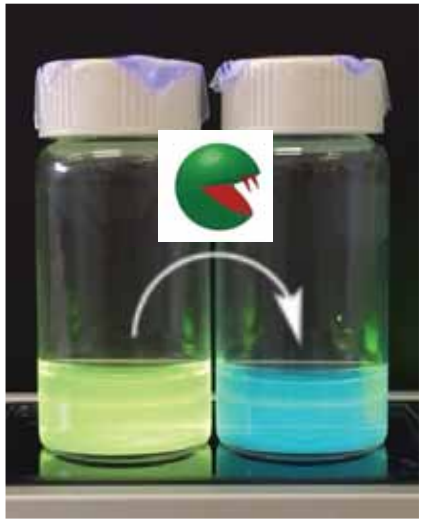
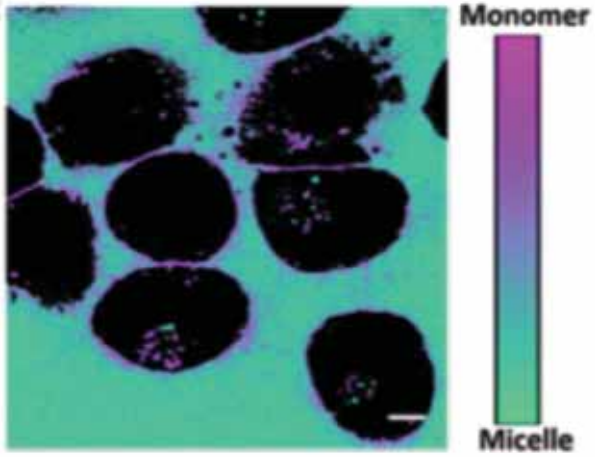
Spectrally active amphiphiles







Fluorescence - Buzhor et al. *Chem. Eur. J,* **2015**, Feiner & Buzhor, *JACS* **2017**

MRI - Buzhor et al. *J. Mat. Chem. B.* **2016**

THERACAT Activities

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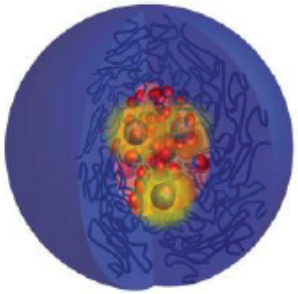
ESR 2 – TAU (Amir)	Micellar catalysts	PhD: Yes	Deliv.: 1.1, 1.2	Start date: M6	Duration 36	WP1

Objectives: **1.** Develop synthetic methodology for amphiphilic polymers with a ligand; **2.** Metal complexation and self-assembly of micelles; **3.** Demonstrating catalytic capability and its optimisation.



Description: ESR2 will develop block-copolymer amphiphiles bearing mono or bivalent ligands at the focal point of the amphiphilic polymer exactly between the hydrophilic and hydrophobic blocks. The ligand will be utilized for complexation of transition metals, which will serve as catalytic centres for the activation of the proposed prodrugs (WP2). Upon their self-assembly in water, these amphiphiles will form polymeric micelles, which will contain high local concentration of catalytic entities at the interface of the hydrophilic shell and the hydrophobic core. The hydrophobic part will be based on dendritic structures due to their high structural precision and modularity, which will allow fine-tuning of the amphiphilicity of the polymers and their micellar stability. Polymers of various compositions will be synthesized and studied (WP1, 3-4)

Planned secondments: GRO – Metal catalyst synthesis (M12, 3 months); **TAG** – in vivo micelle imaging (M32, 4 months).	**Expected results (deliverables)**: Polymeric amphiphiles with metal binding ligands (D1.1); metal containing polymeric micelles (D1.2); Micelles with catalytic activity (D1.2)

THERACAT deliverables for ESR 2

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D1.1: Polymeric amphiphiles with metal binding ligands

D1.2: Metal containing polymeric micelles

D1.3: Micelles with catalytic activity (catalytic activation of anti-cancer prodrugs).

Shreyas Wagle

THERACAT goals for ESR 2

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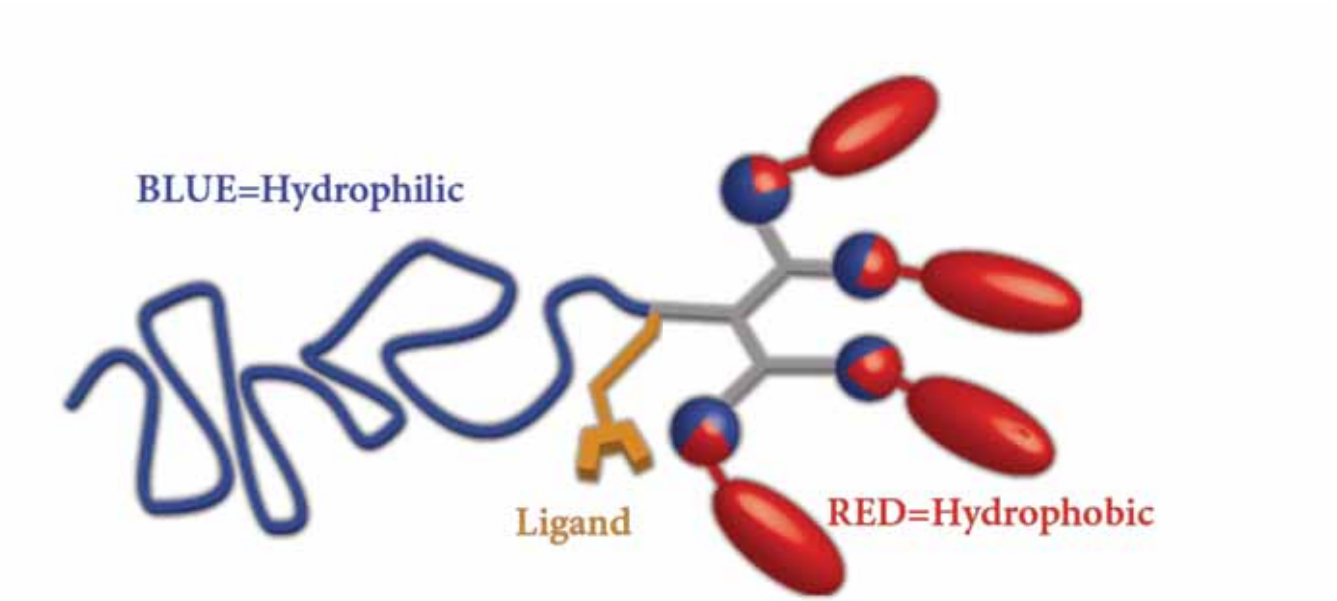
1. **Develop synthetic methodology for amphiphilic polymers with a ligand**



THERACAT goals for ESR 2

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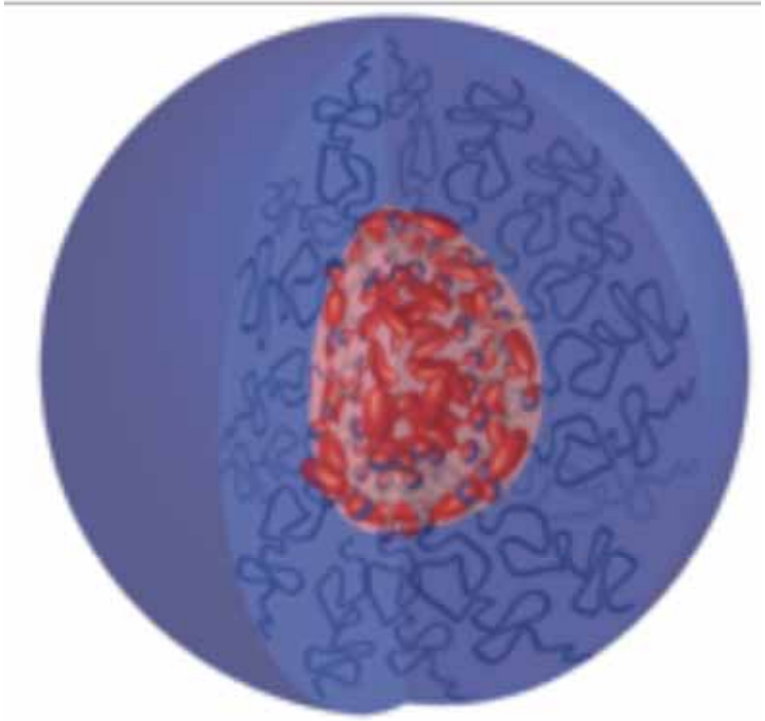
2. Metal complexation and self-assembly of micelles



THERACAT goals for ESR 2

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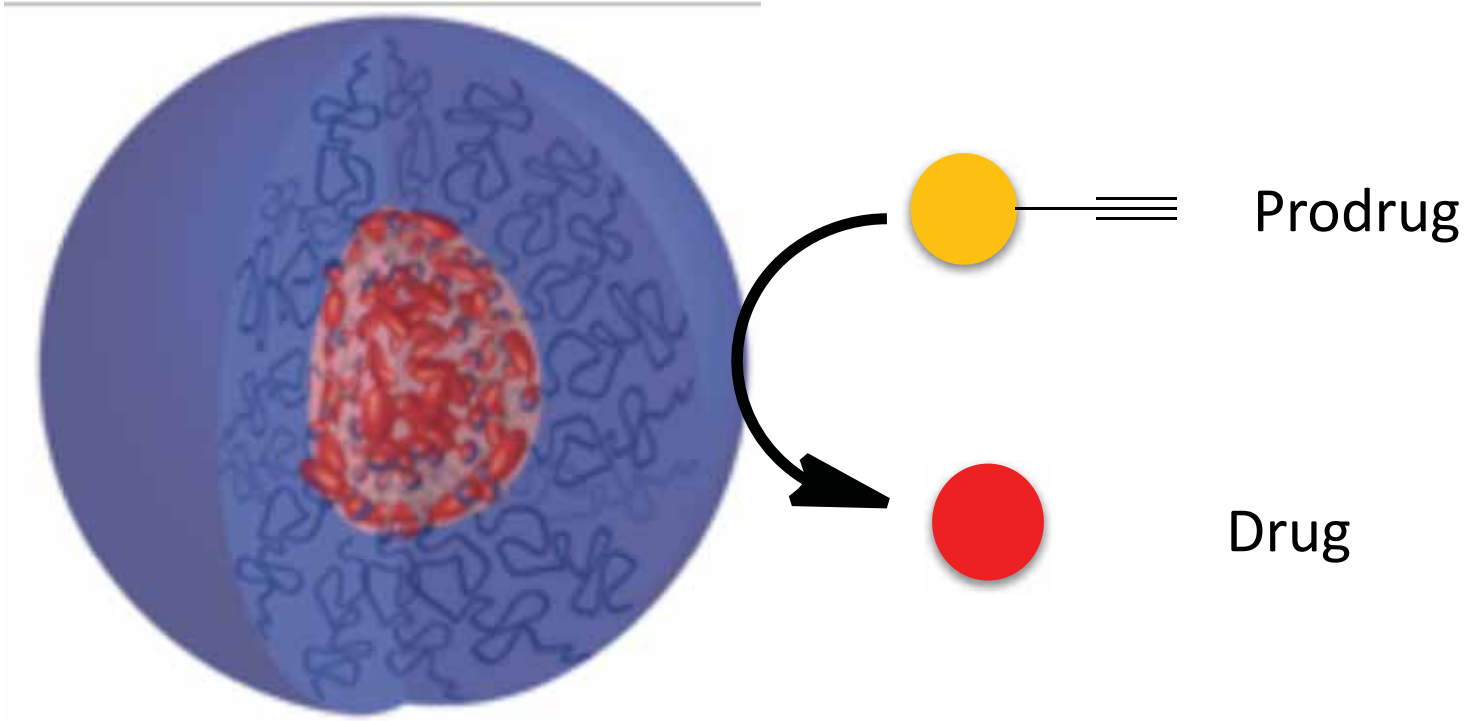
3. Demonstrating catalytic capability and its optimization



THERACAT Activities

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Training Courses:

Designing delivery systems: concepts, examples and concerns
Month 24

Hosting ESR 5 (Month 34 for 3 months)

Hosting training event 4 and ESR meeting 3
(Month 30)