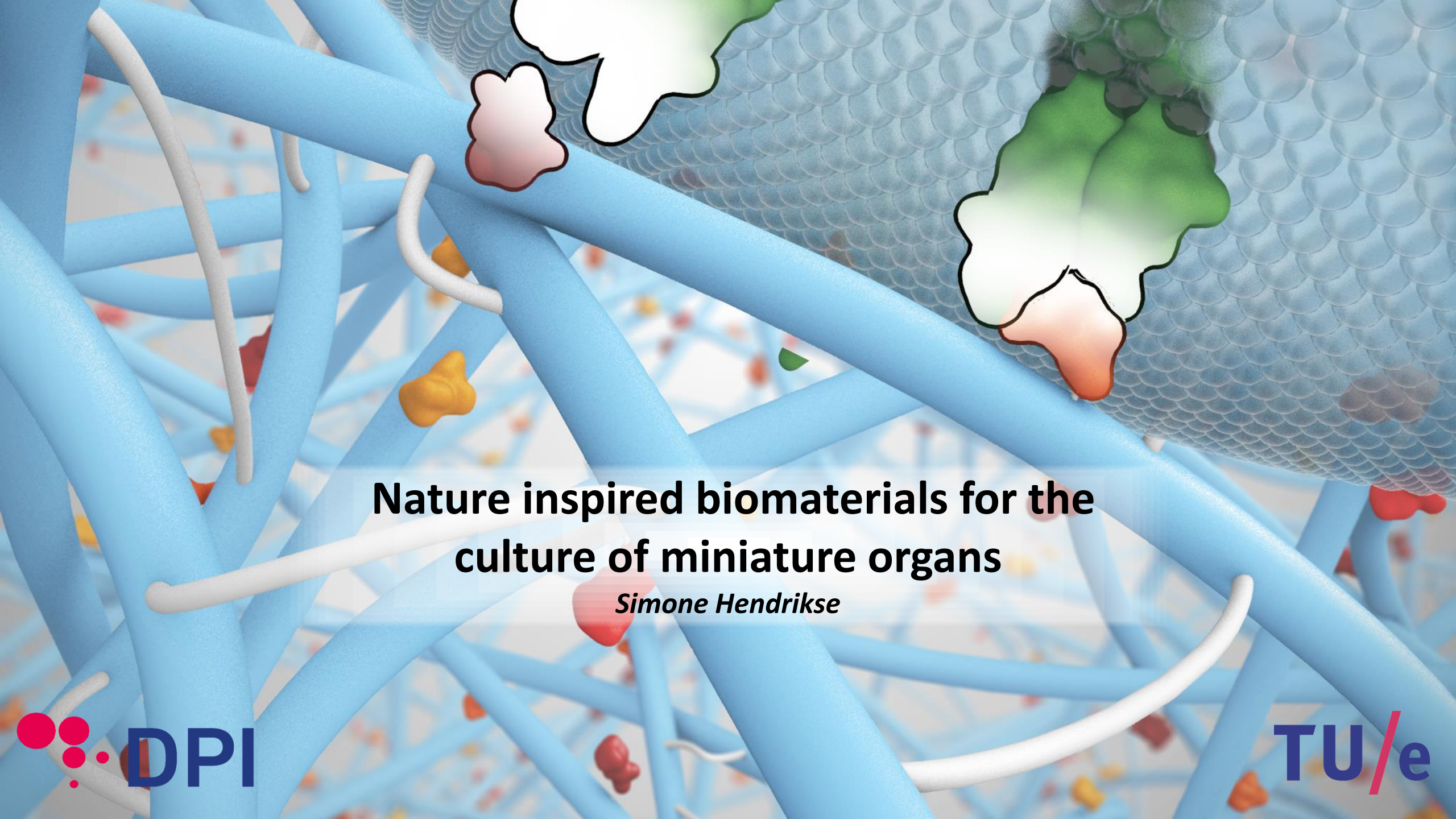


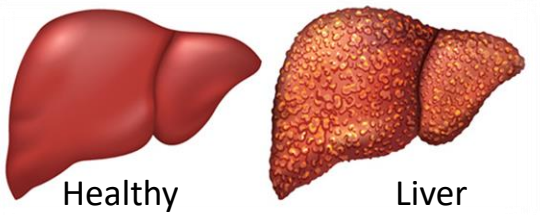
Nature inspired biomaterials for the culture of miniature organs

Simone Hendrikse

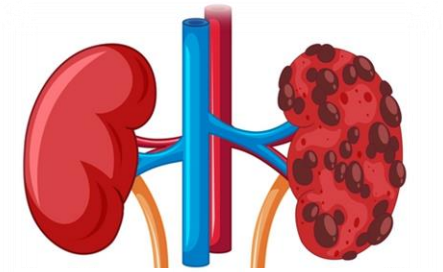
DPI

TU/e

Thousands of people suffer from organ failure

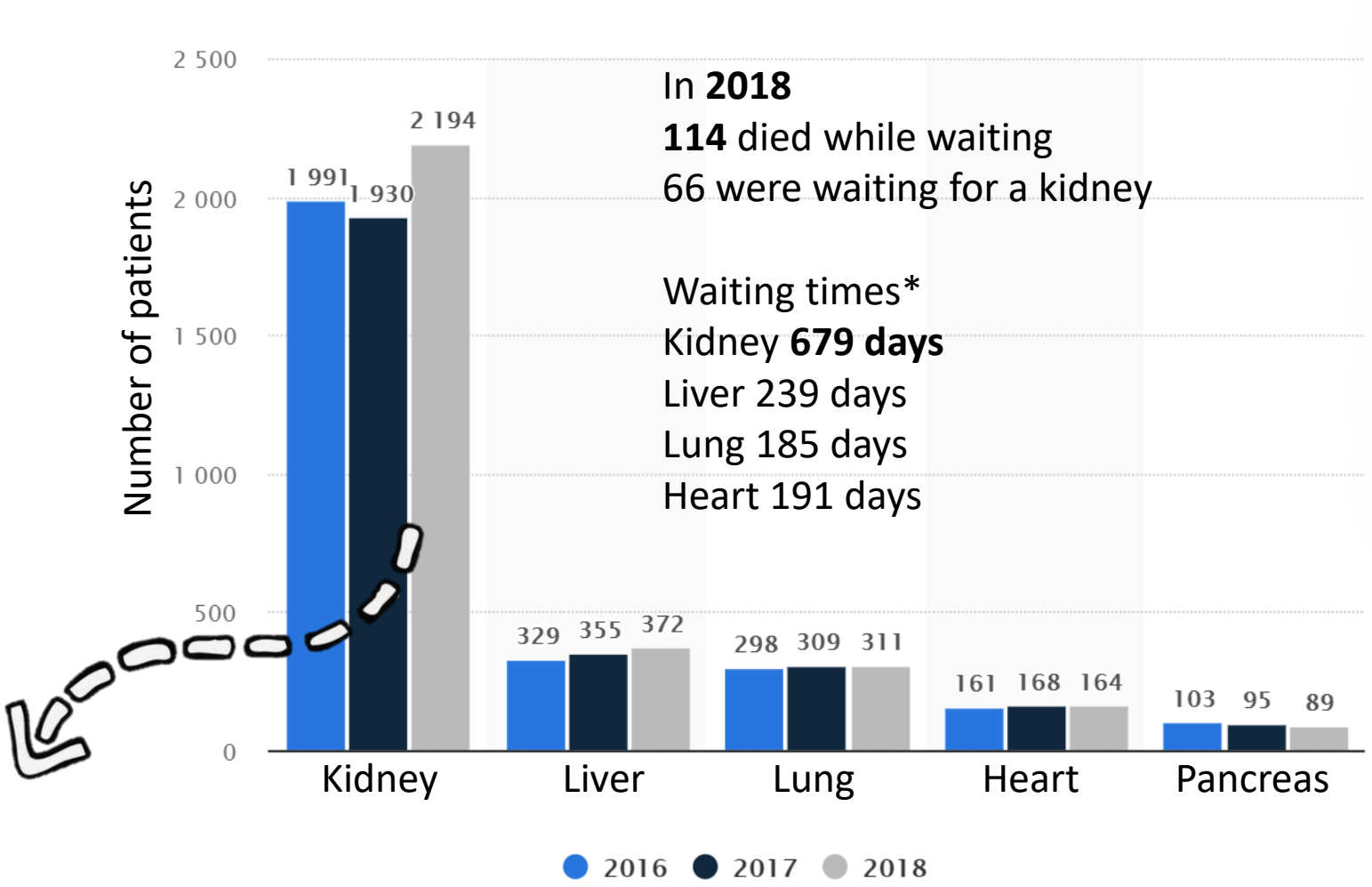


Healthy Liver | Liver Cirrhosis



Healthy Kidney | Polycystic Kidney

Number of patients on waiting list in the Netherlands

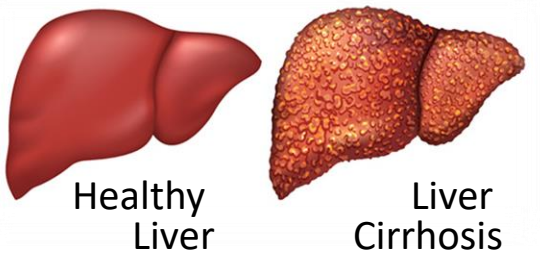


In **2018**
114 died while waiting
66 were waiting for a kidney

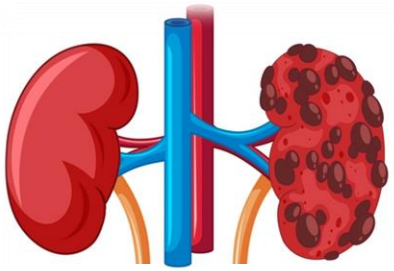
Waiting times*
Kidney **679 days**
Liver 239 days
Lung 185 days
Heart 191 days

* In U.S. in 2017

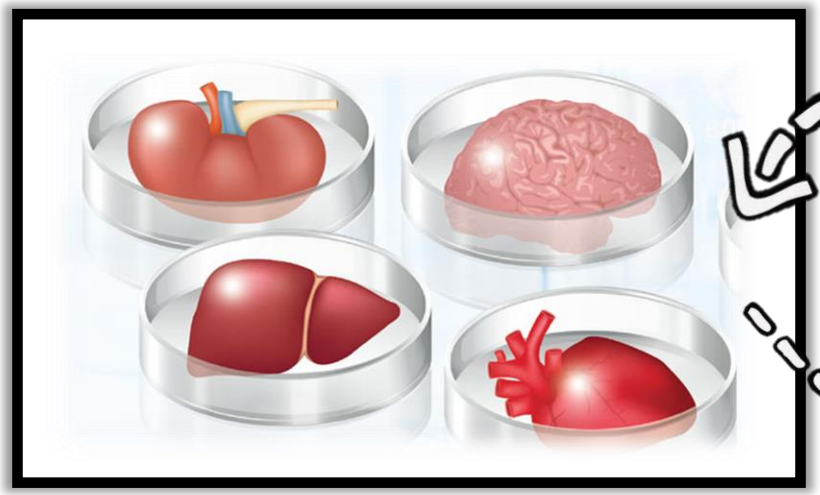
Thousands of people suffer from organ failure



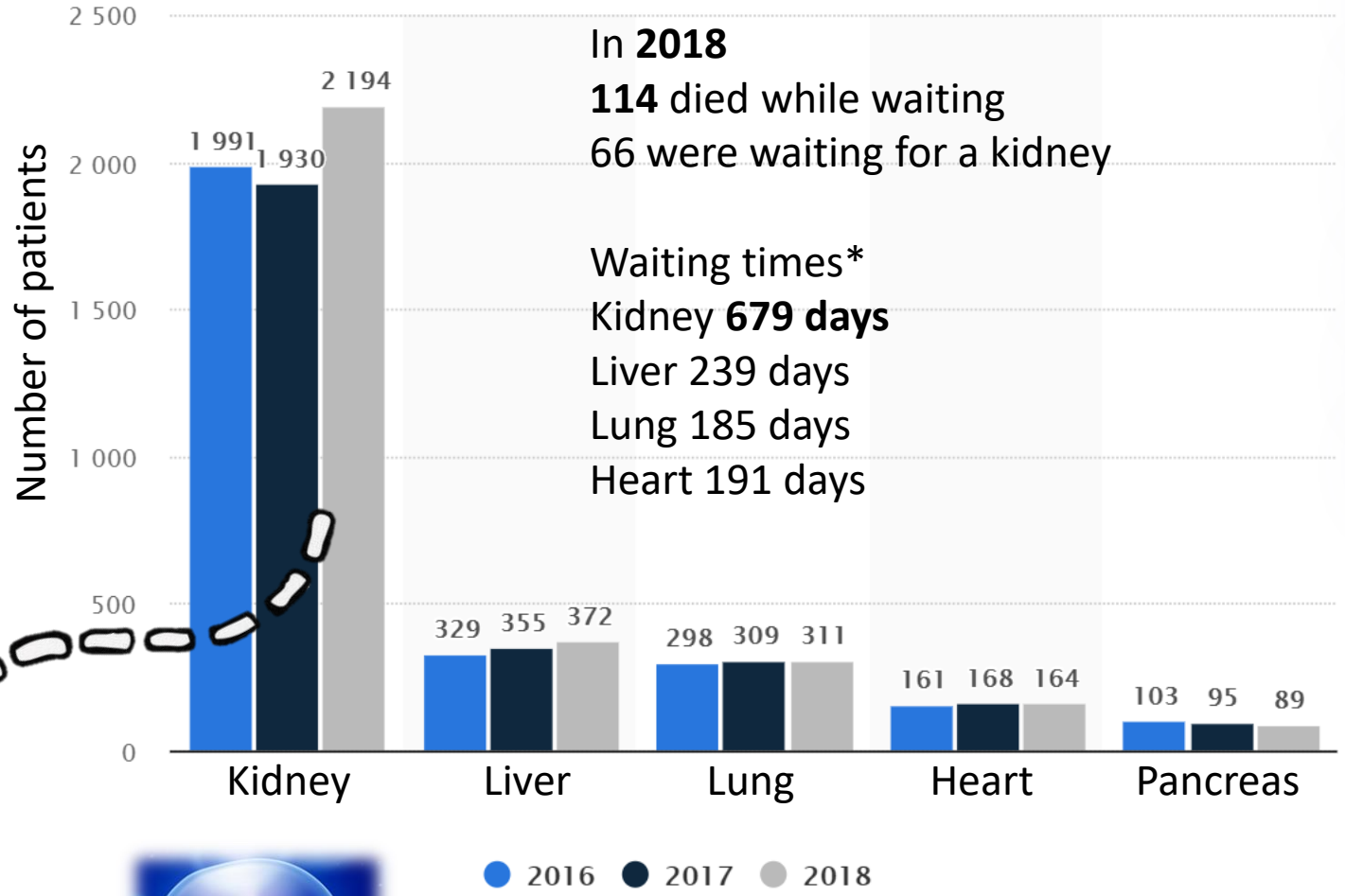
Healthy Liver | Liver Cirrhosis



Healthy Kidney | Polycystic Kidney



Number of patients on waiting list in the Netherlands



In **2018**
114 died while waiting
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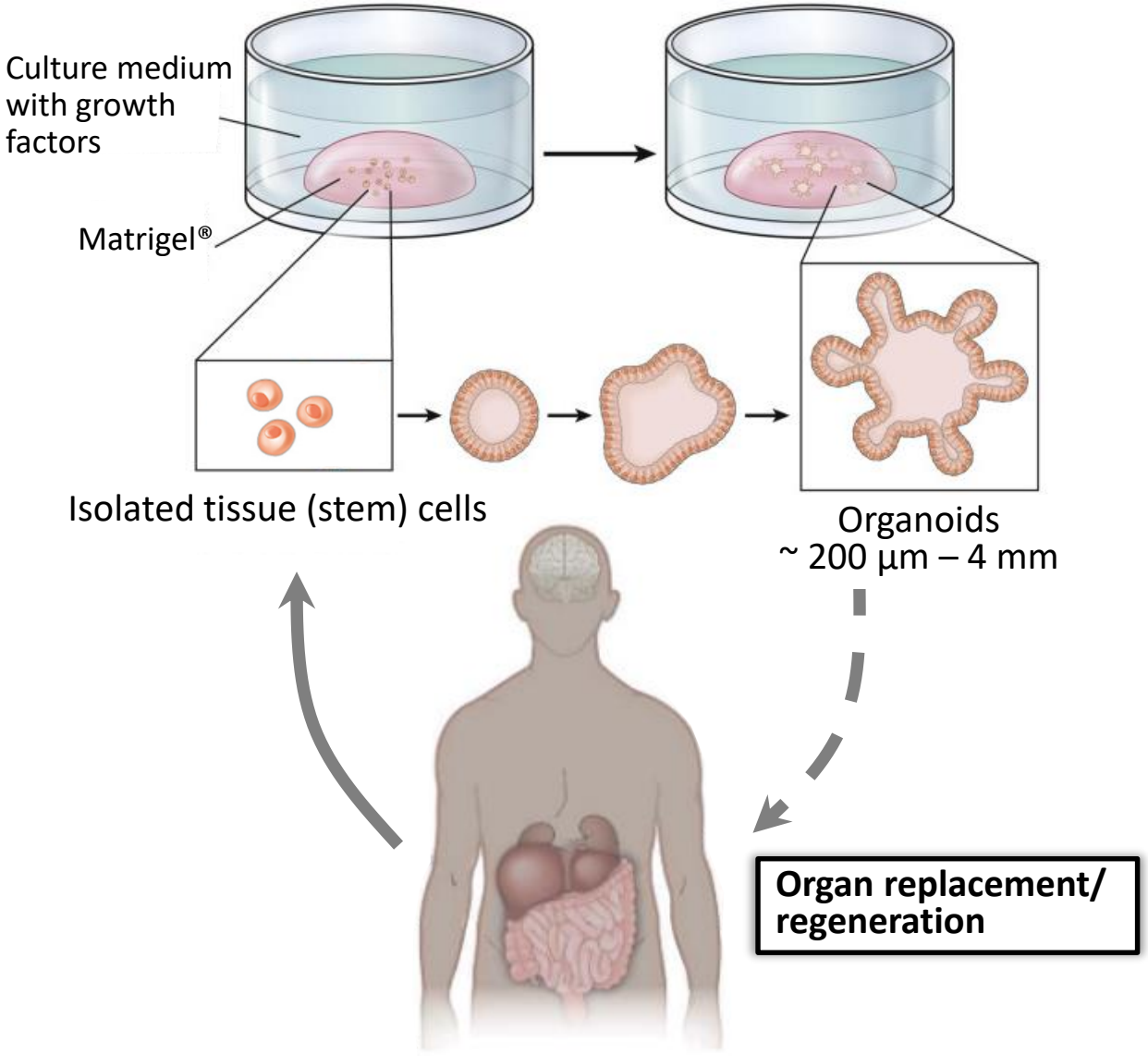
Waiting times*
Kidney **679 days**
Liver 239 days
Lung 185 days
Heart 191 days

Patient-derived cells?

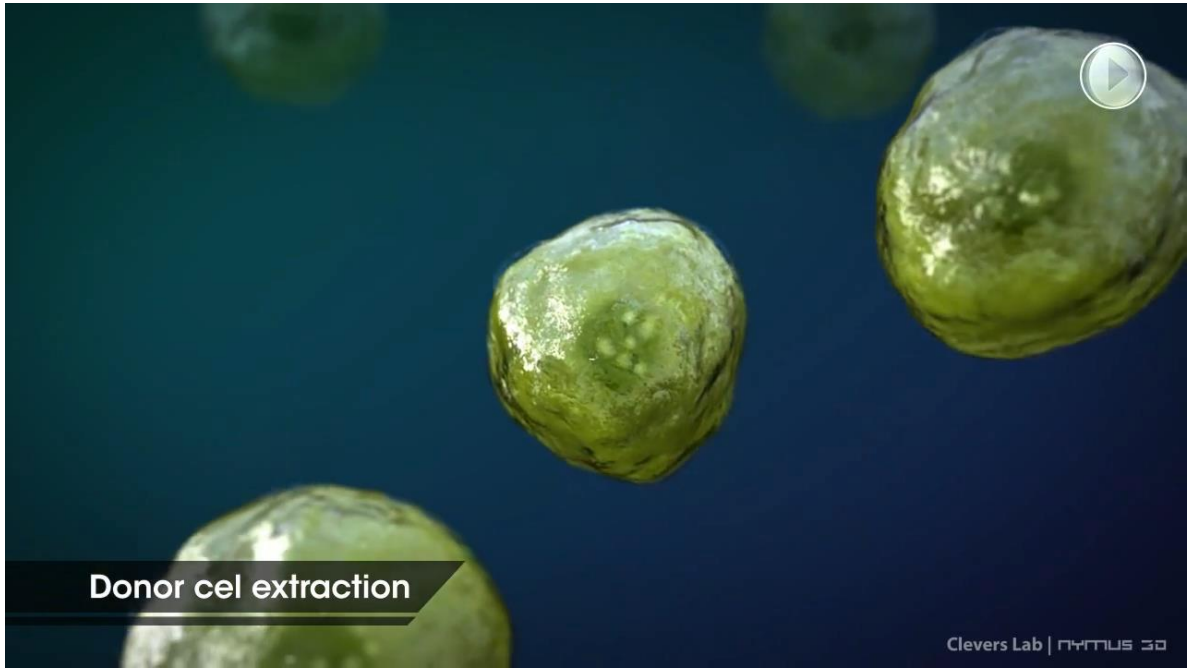
* In U.S. in 2017

Organoids for regenerative medicine still hindered by Matrigel® dependence



- Hydrogel containing **~1850 proteins**
- Extracted from **tumour** mice
- Batch-to-batch **variation**

- **Not well-defined and possibly pathogenic**

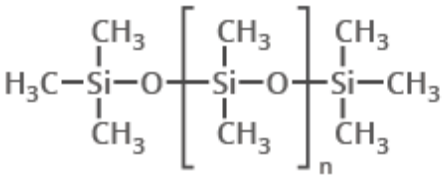


Fujii. *Gastroenterology* **156** (3), 562 – 576 (2018)

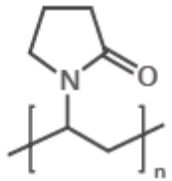
Successful hydrogels already on the market

- Hydrogels are water-swollen 3D polymeric networks

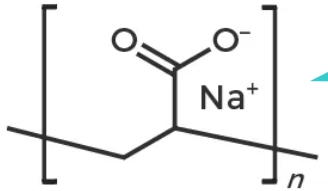
Contact Lenses



POLYDIMETHYLSILOXANE



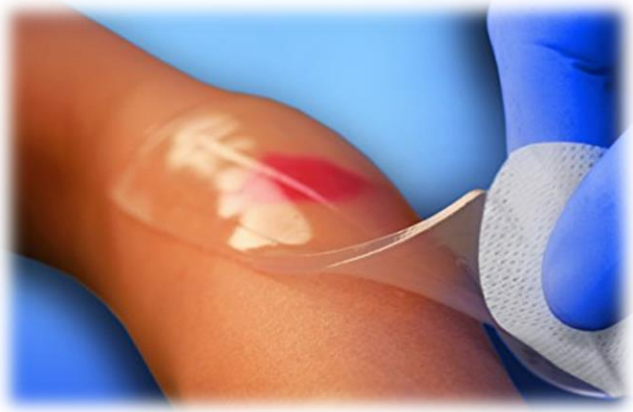
POLYVINYLPYRROLIDONE

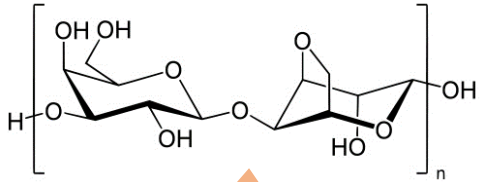


SODIUM POLYACRYLATE

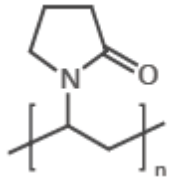
Disposable Nappies

Wound Dressing





AGAR



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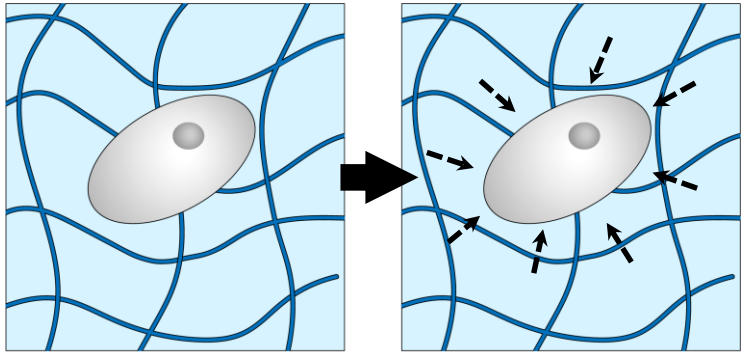
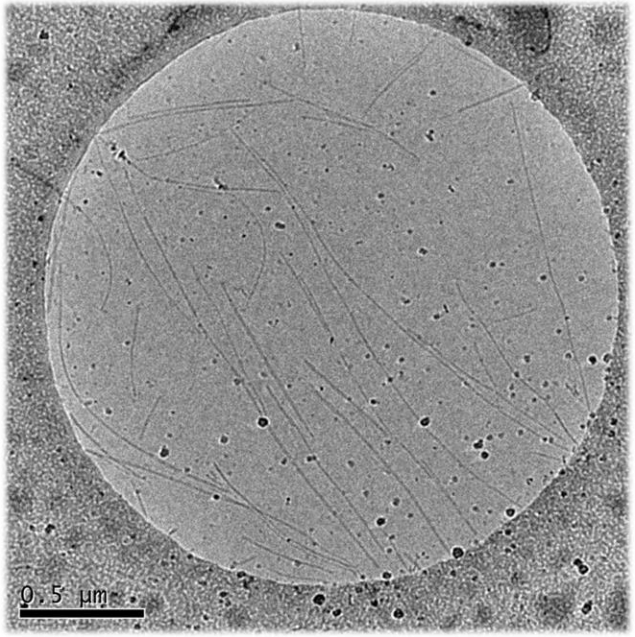
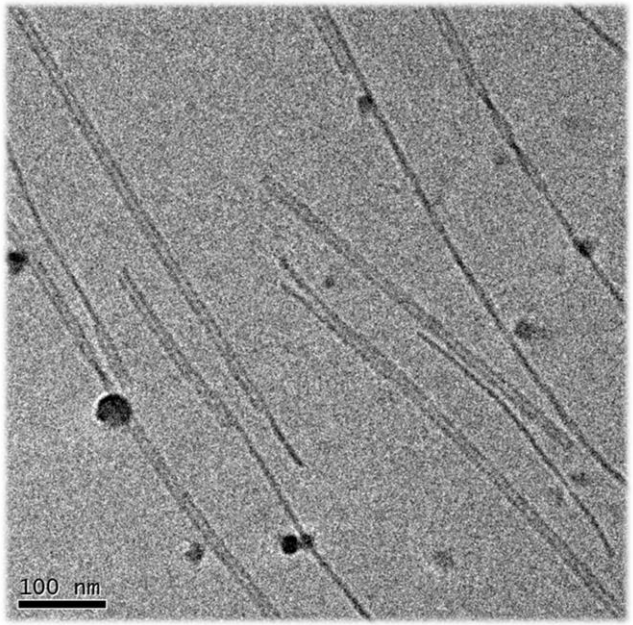


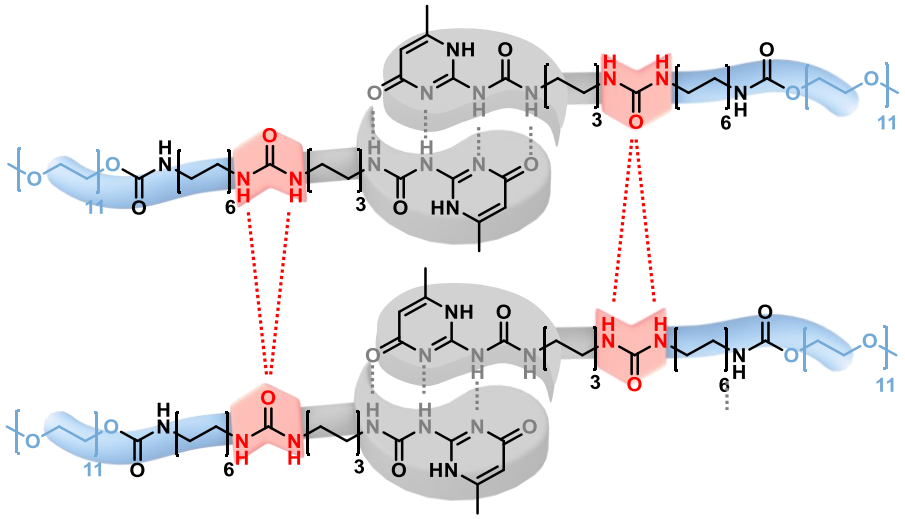
- Impedes cell growth

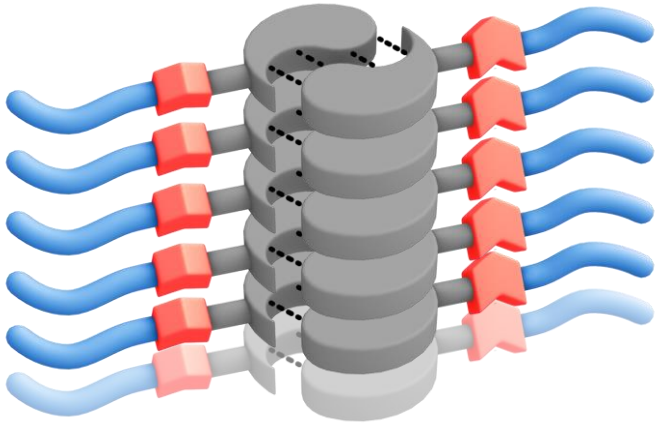
Biomimicry of dynamic fibrous structures found in and outside cells

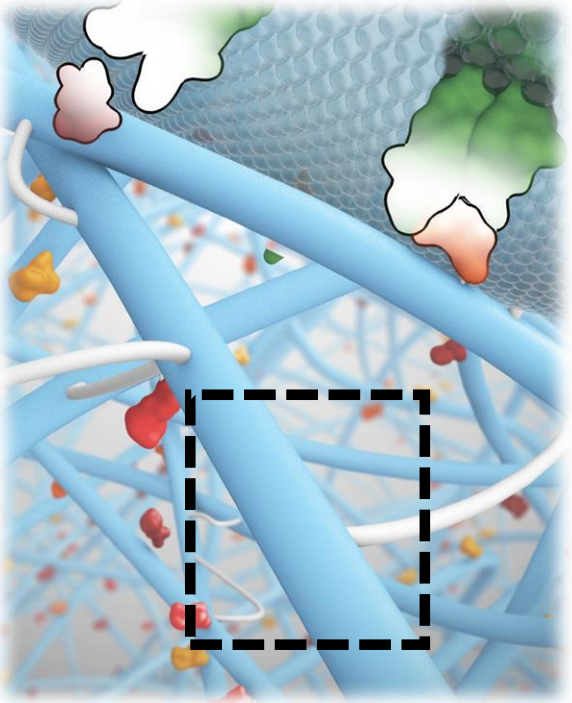


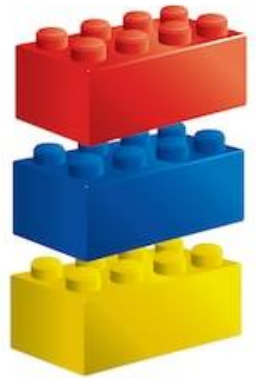


Ureidopyrimidinone (UPy)





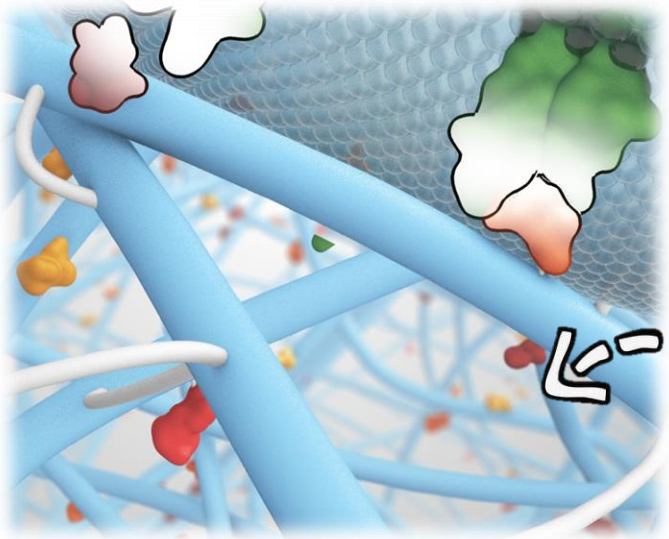




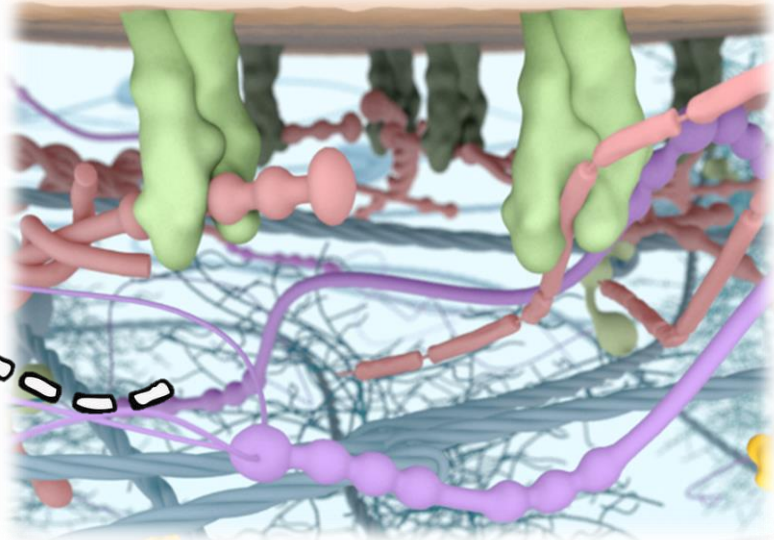
Aim of the PhD thesis

Develop a multi-component hydrogel as synthetic **Matrigel replacement** for the expansion of organoids

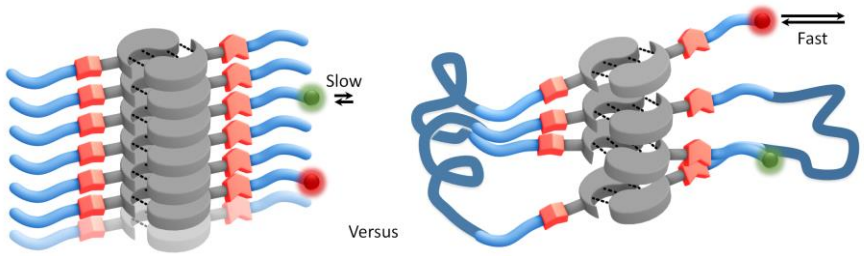
Synthetic ECM

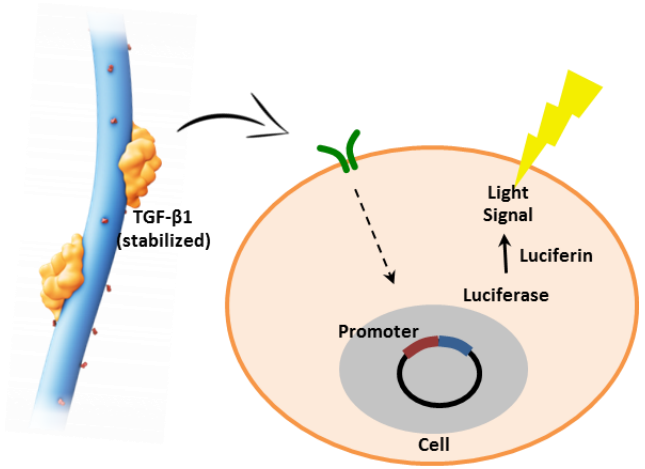


Natural ECM



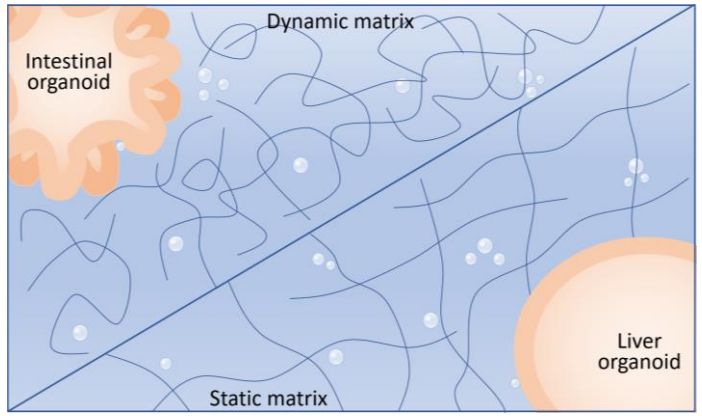
1. Fundamental studies



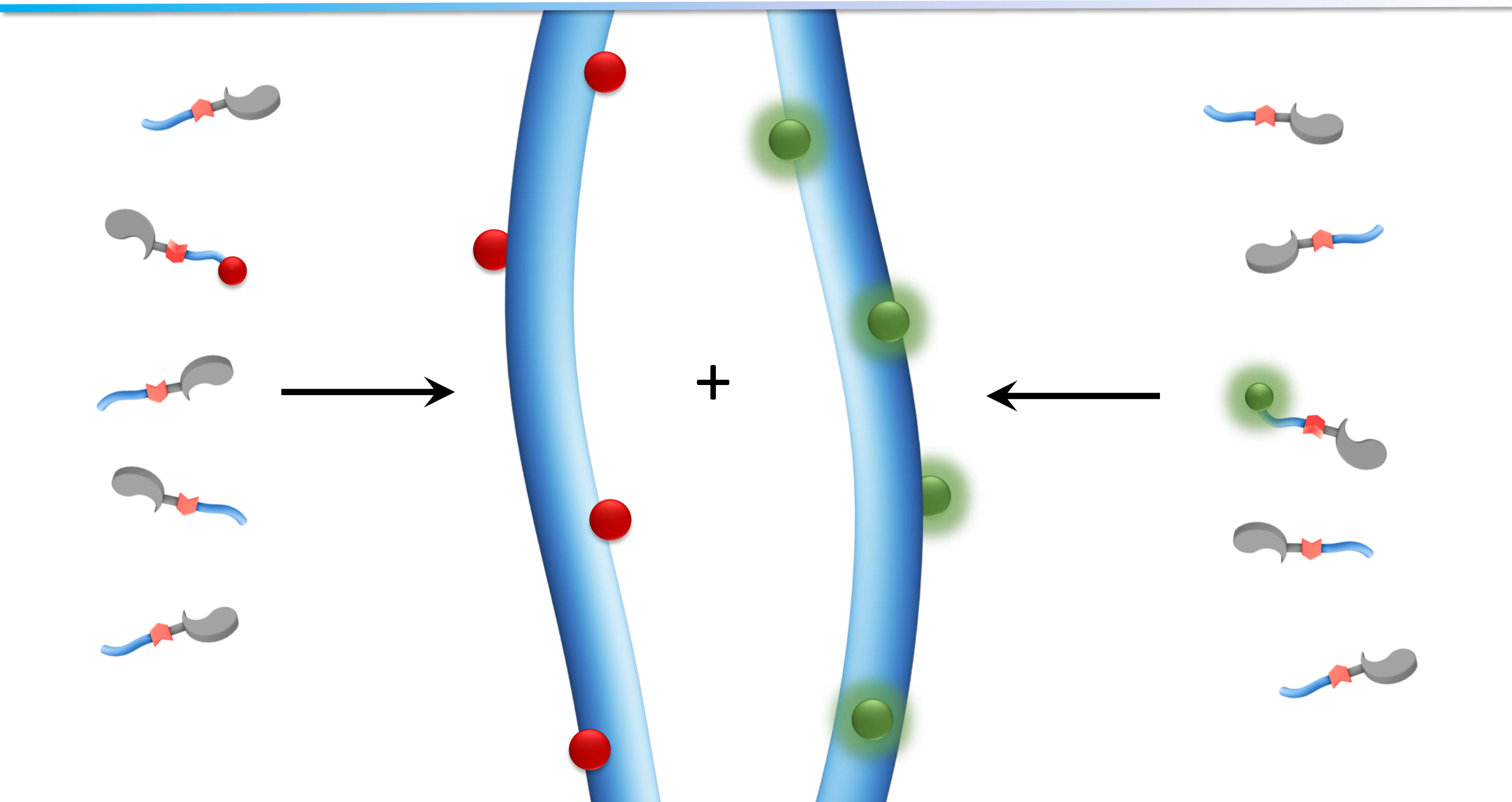


2. Incorporating functionality

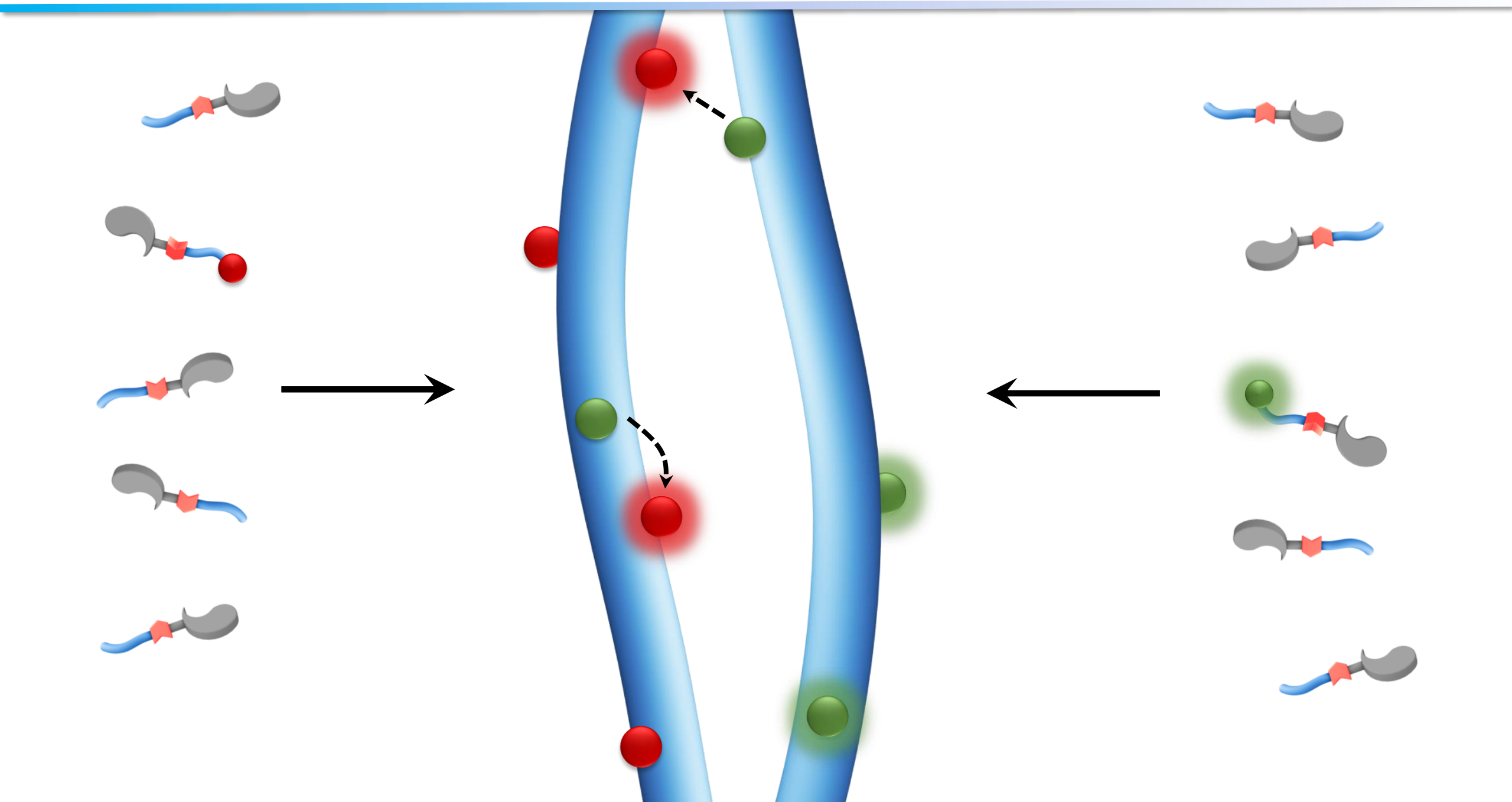
3. Cell experiments



1. Fundamental studies: Investigating the internal dynamics



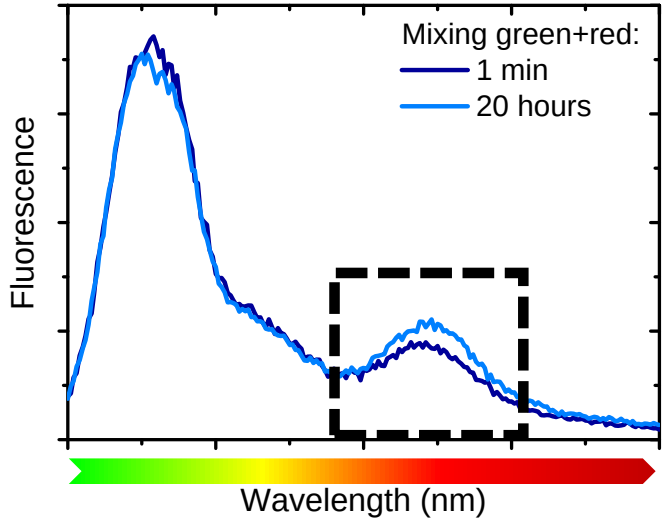
1. Fundamental studies: Investigating the internal dynamics



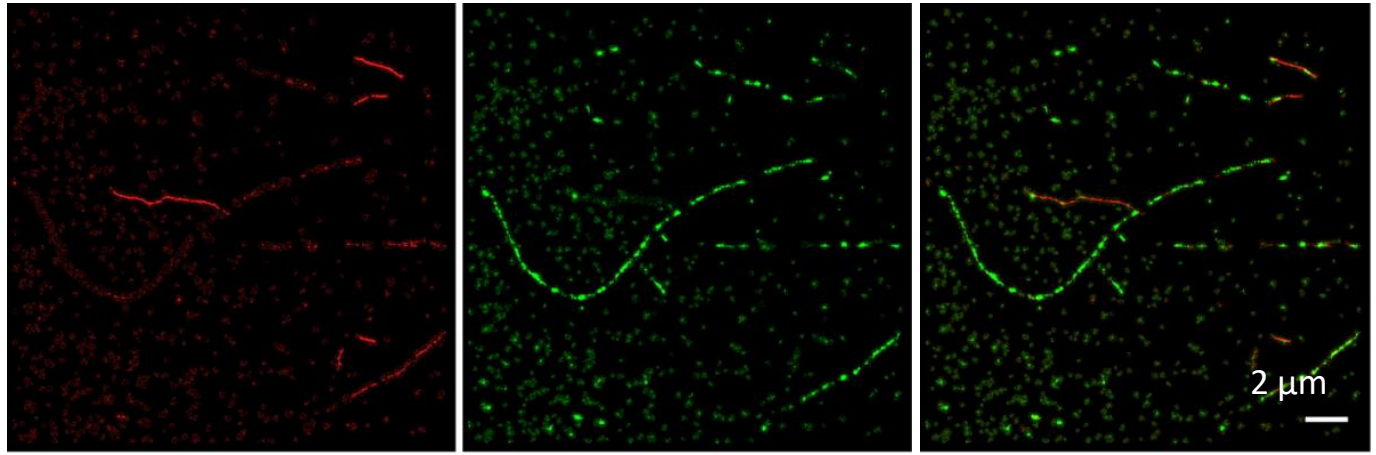
1. Fundamental studies: Molecular design dictates dynamic profile

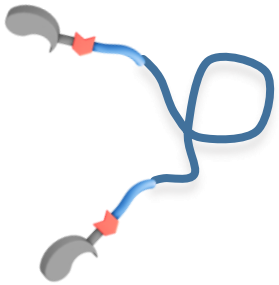
mUPy

➢ Slow exchange



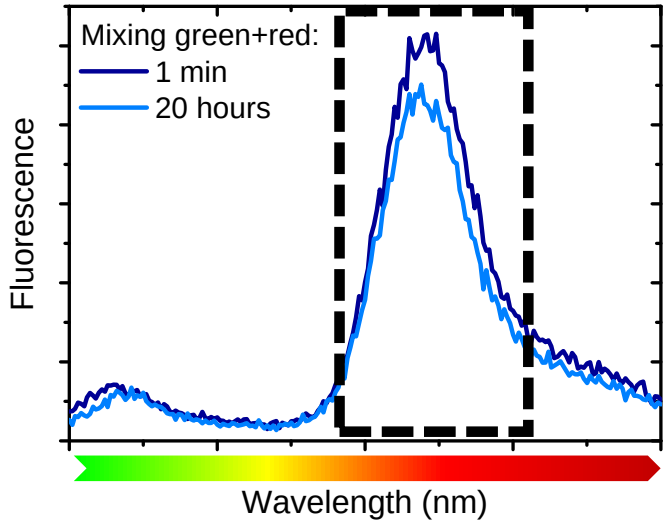
Red Channel | Green channel | Merged



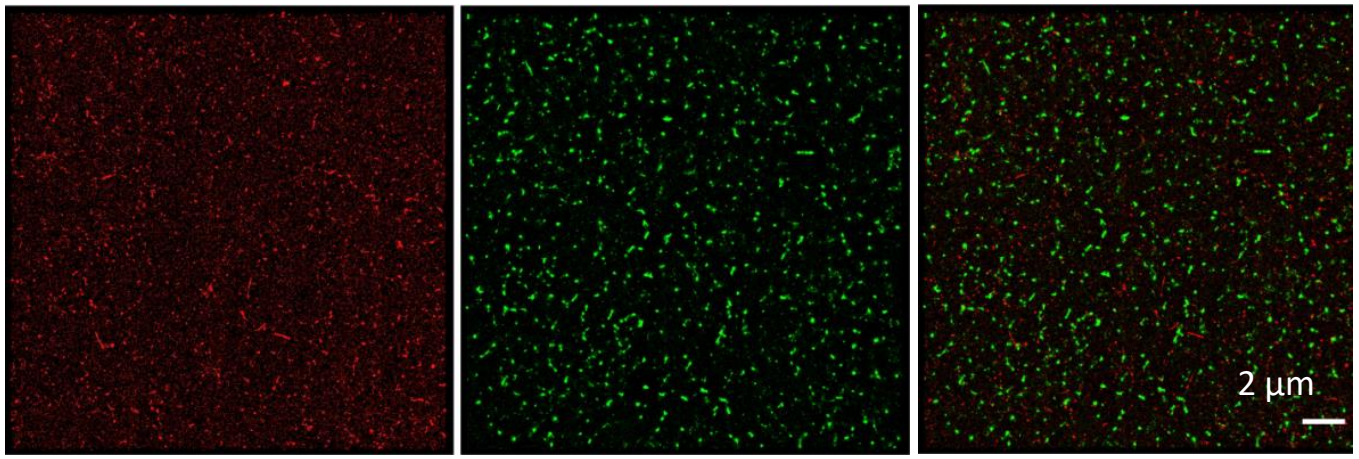


bUPy

➢ Fast exchange



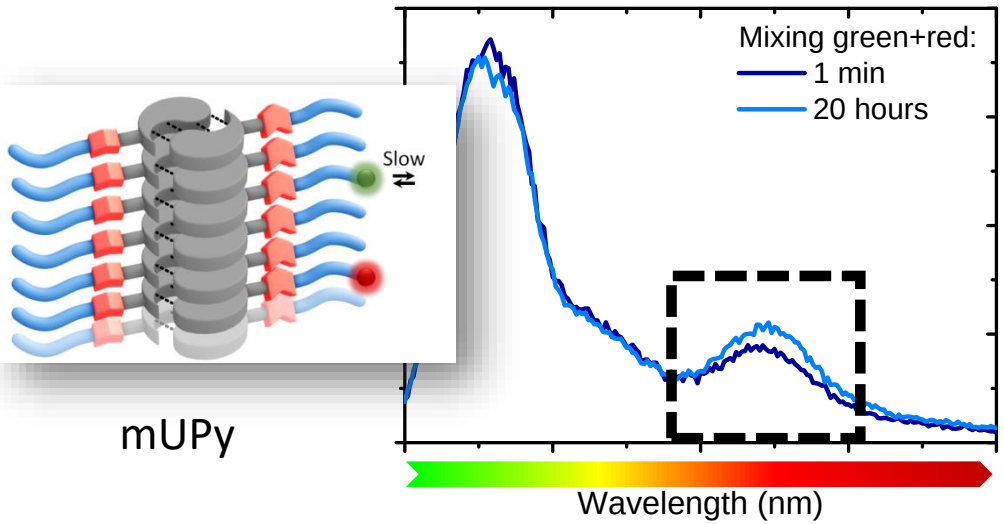
Red Channel | Green channel | Merged



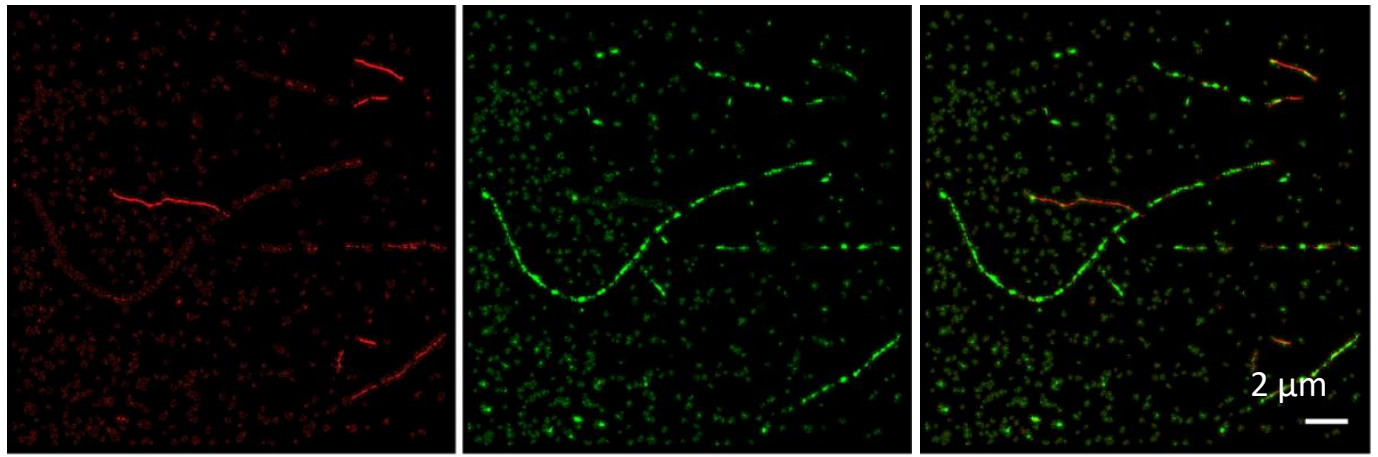
Hendrikse, et al. *Chem. Commun*. **53**, 2279-2282 (2017)

1. Fundamental studies: Molecular design dictates dynamic profile due to molecular packing

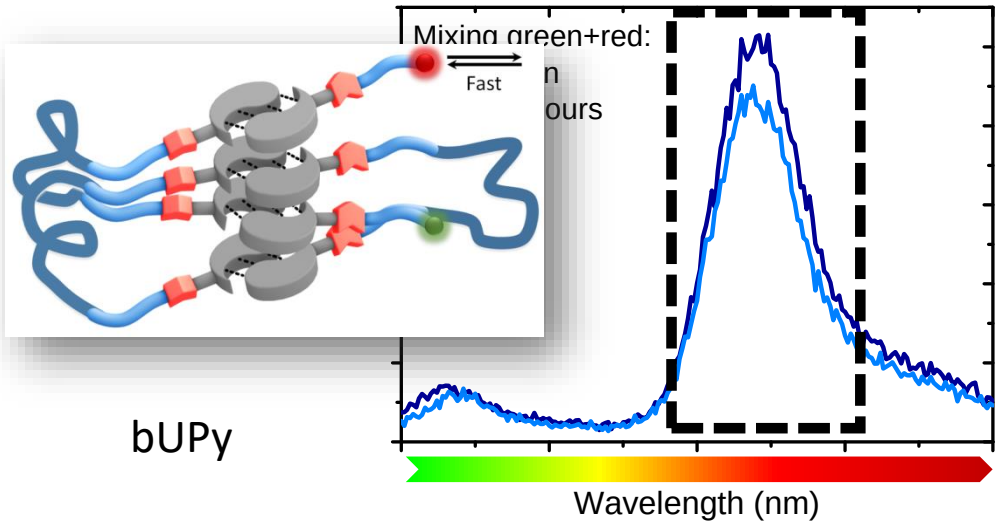
➢ Slow exchange



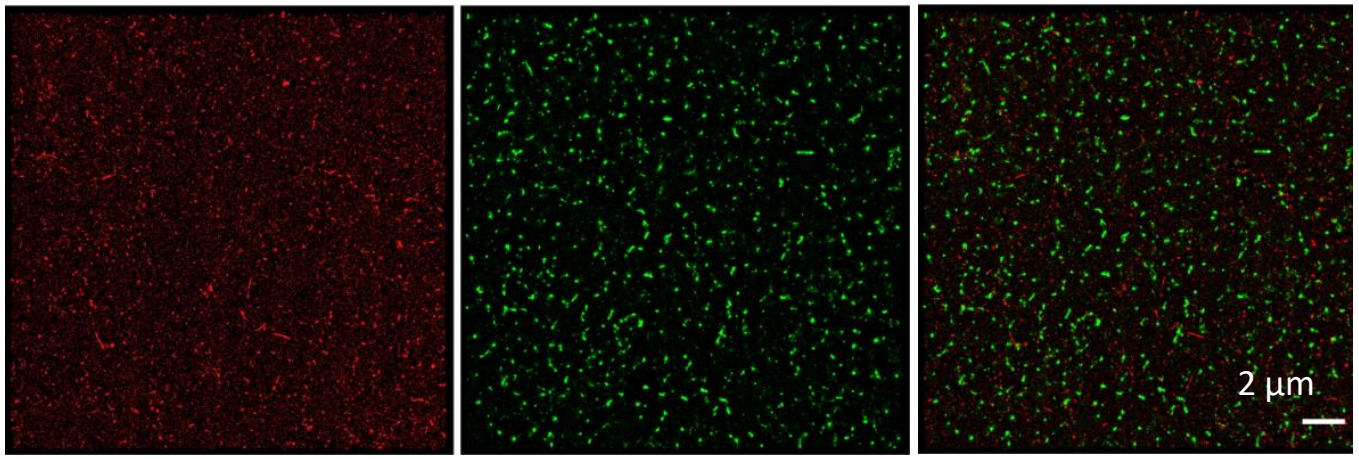
Red Channel | Green channel | Merged



➢ Fast exchange

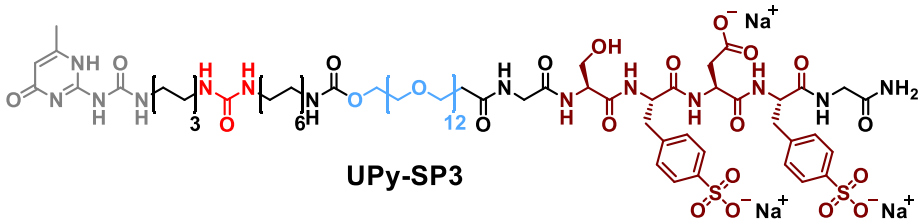


Red Channel | Green channel | Merged



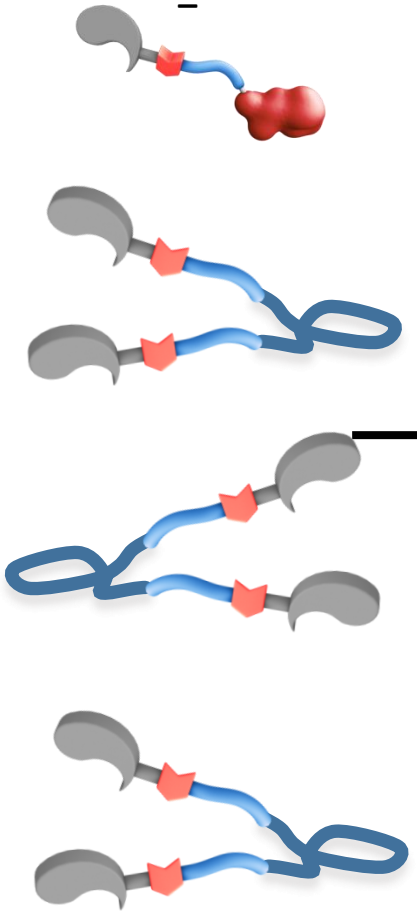
Hendrikse, et al. *Chem. Commun*. **53**, 2279-2282 (2017)

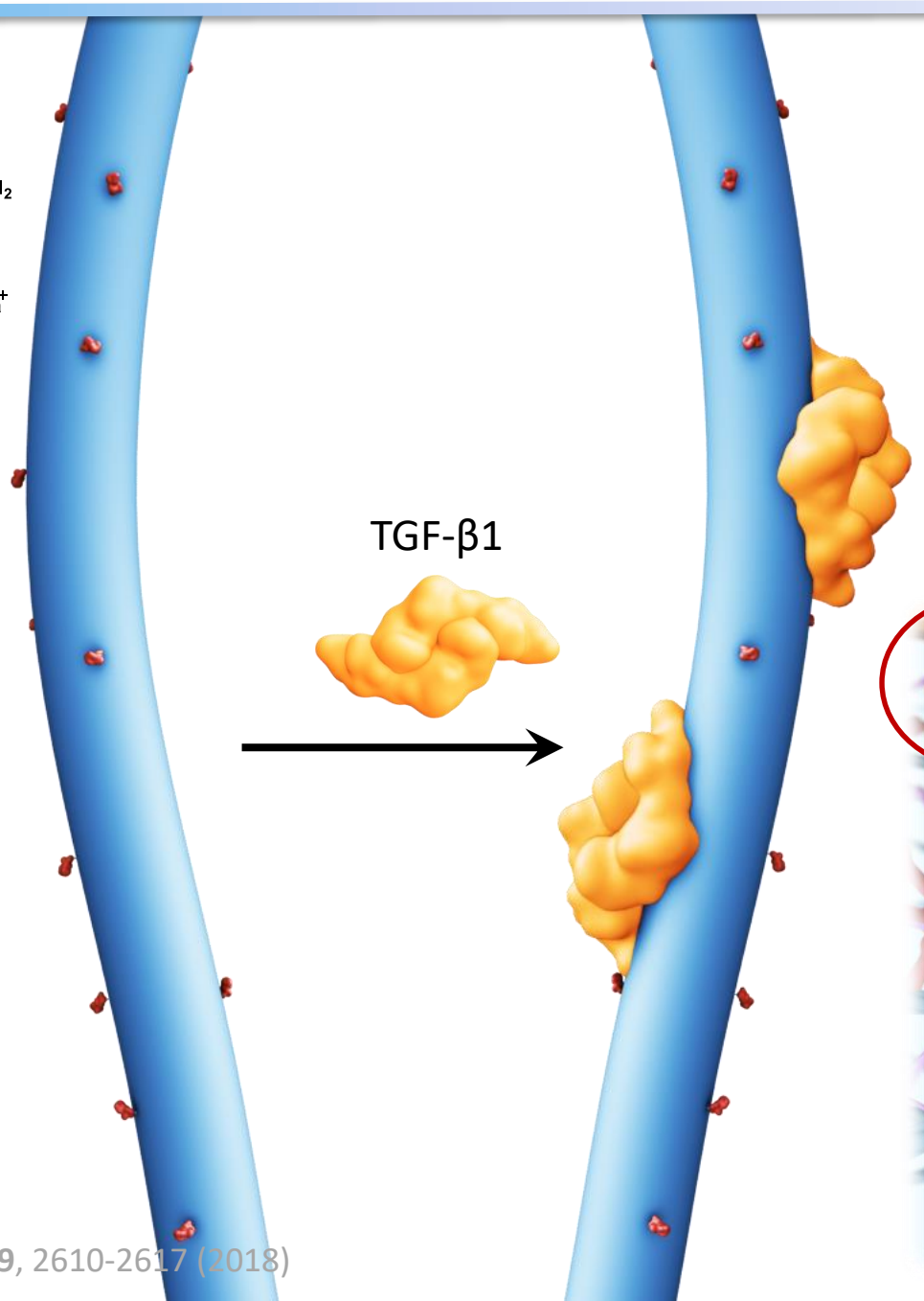
2. Functionality: Growth factor immobilization and stabilization



UPy-SP3

≡

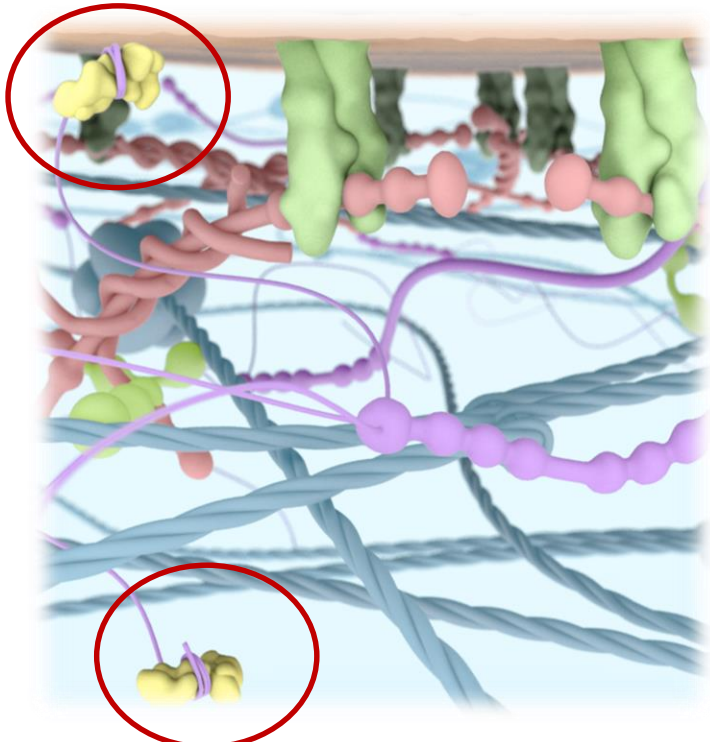




TGF-β1

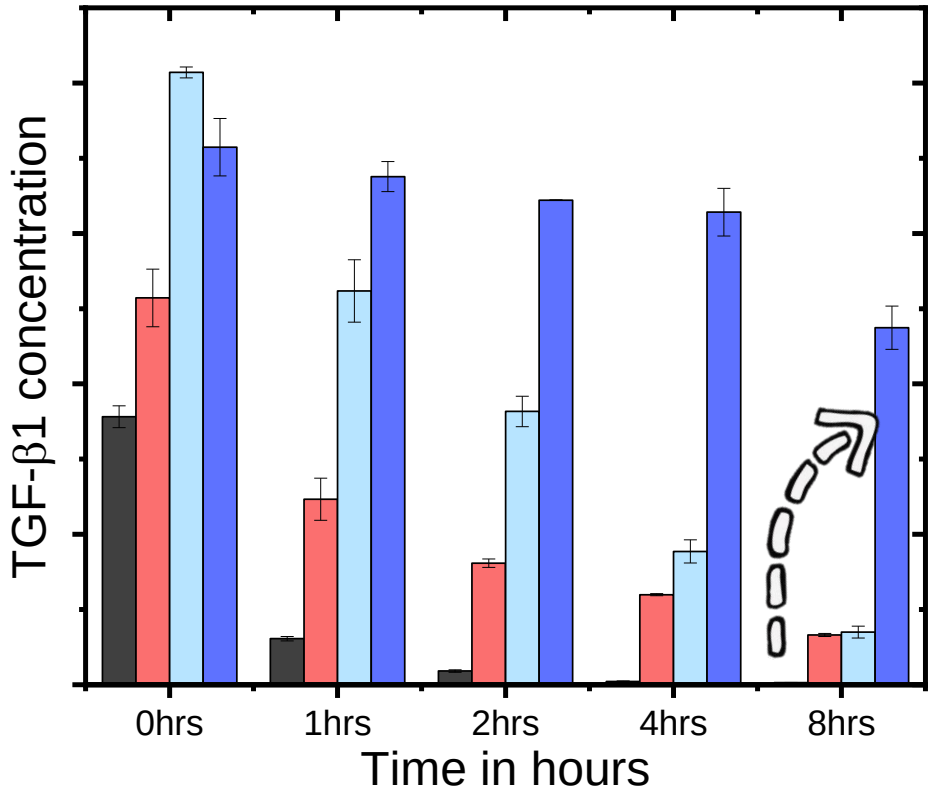
TGF-β1

1 mg
$ 5,200

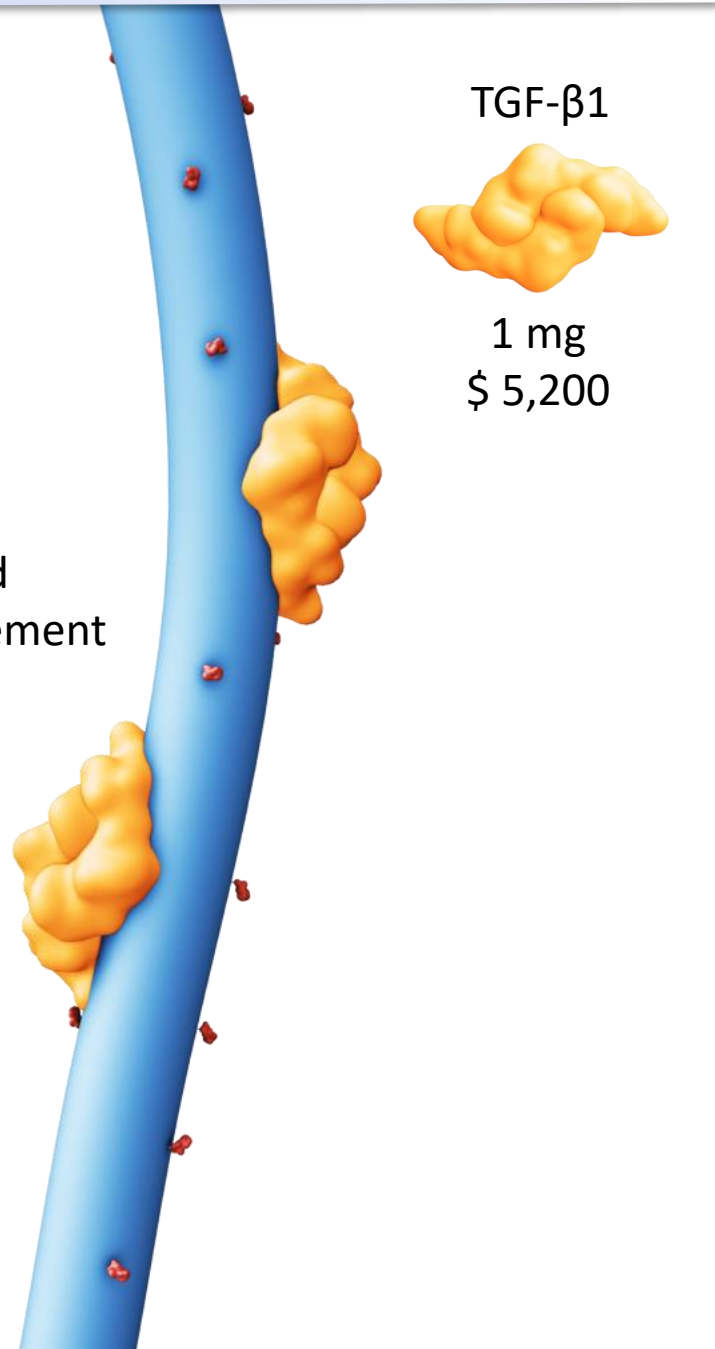


Hendrikse, Spaans, Meijer, Dankers. *Biomacromolecules*, **19**, 2610-2617 (2018)

2. Functionality: Supramolecular polymers stabilize TGF-β1 over several hours



178 Fold improvement

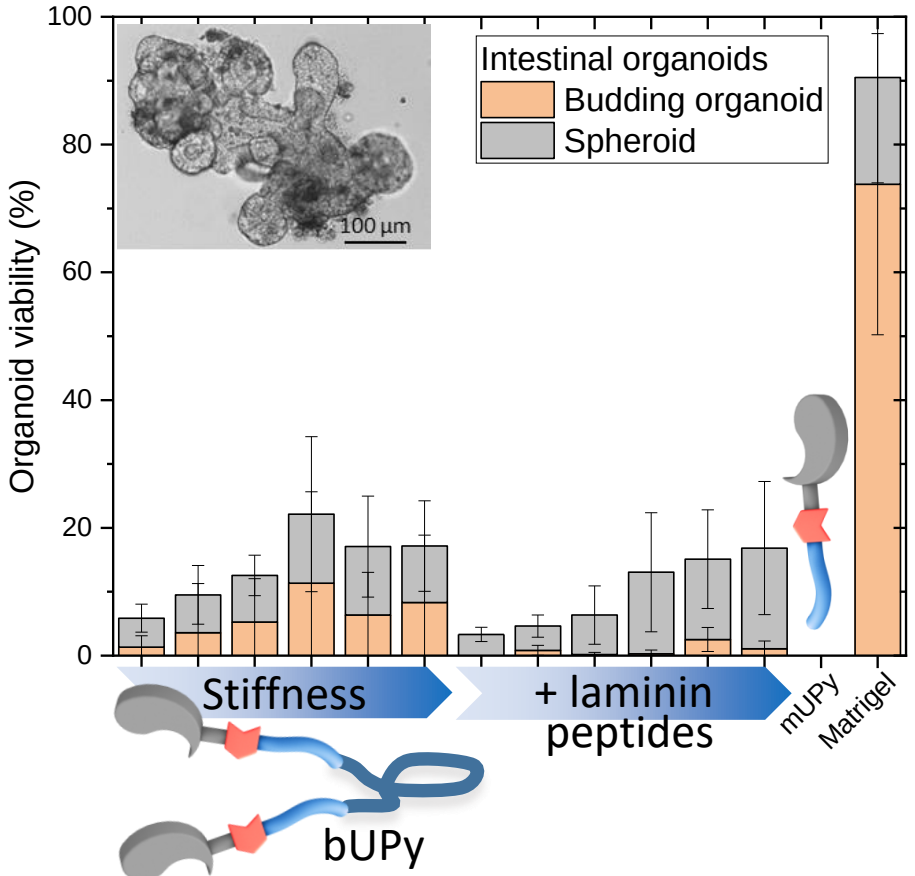


TGF-β1

1 mg
$ 5,200

Hendrikse, Spaans, Meijer, Dankers. *Biomacromolecules*, **19**, 2610-2617 (2018)

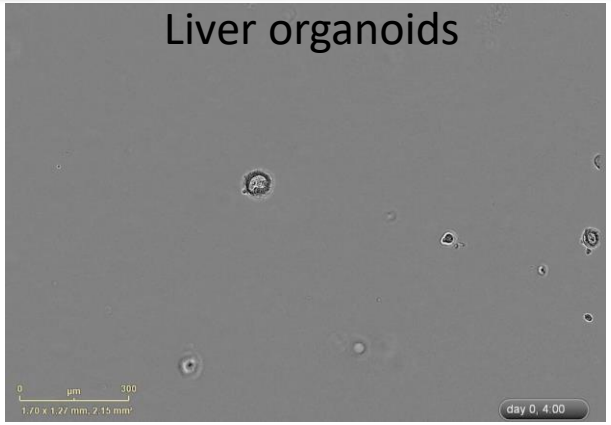
3. Organoid experiments: intestinal versus liver organoids

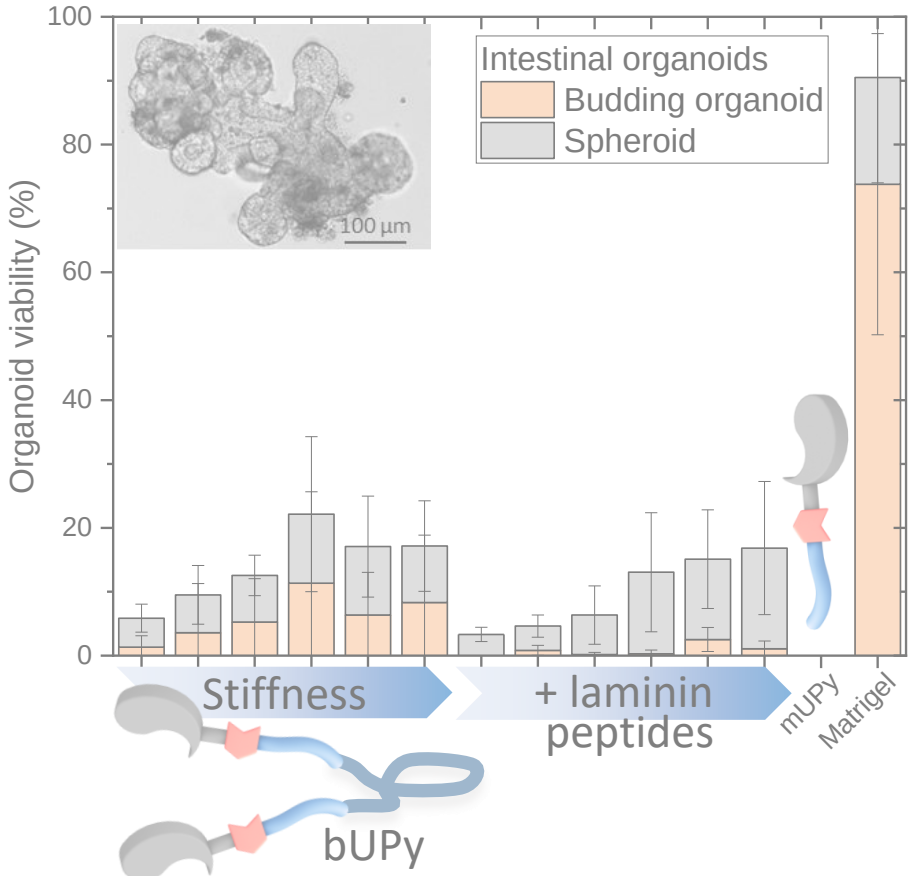


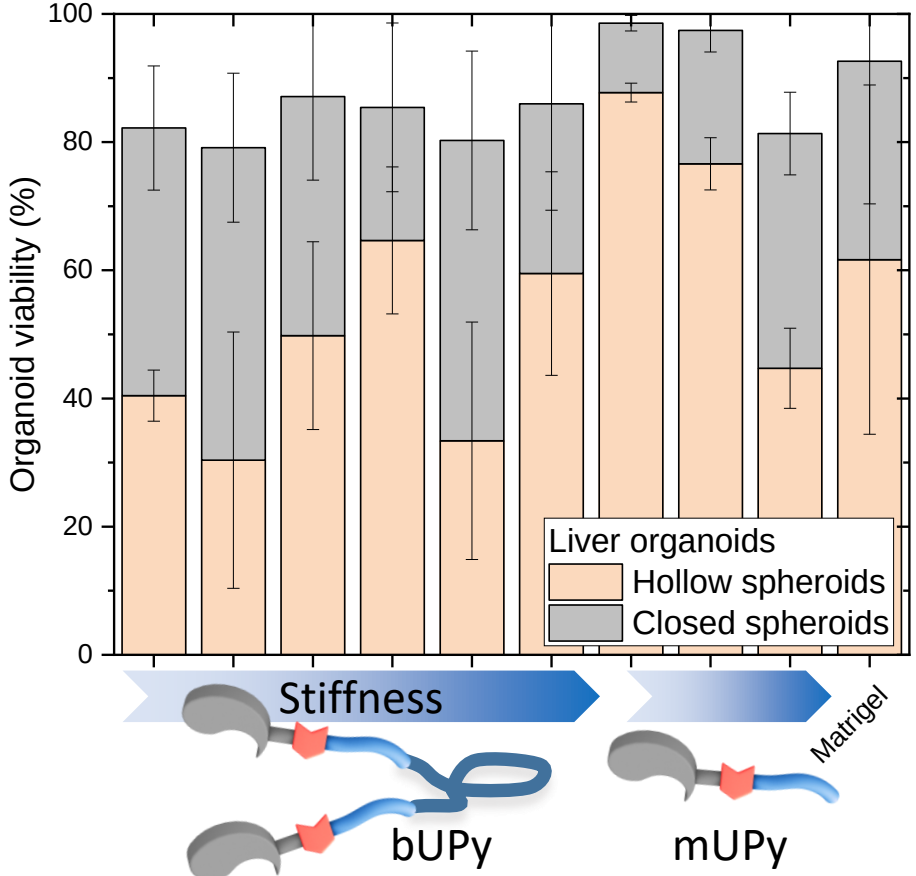
Matrigel®

In collaboration with Hans Clevers lab, Utrecht

3. Organoid experiments: intestinal versus liver organoids



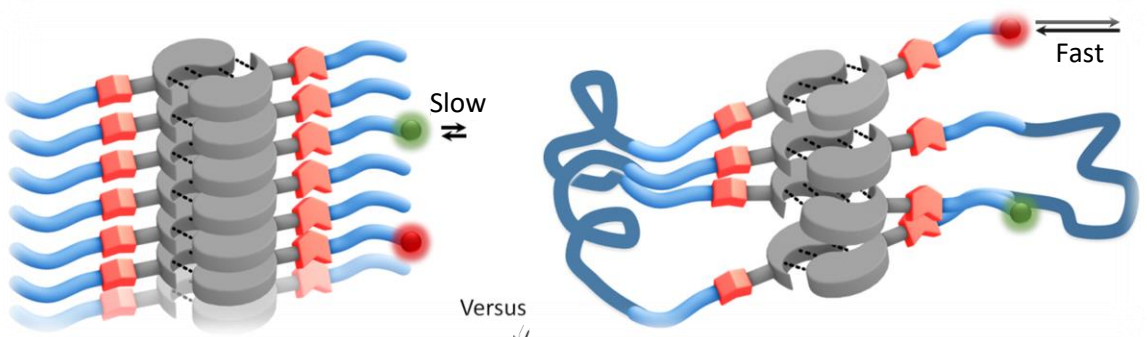




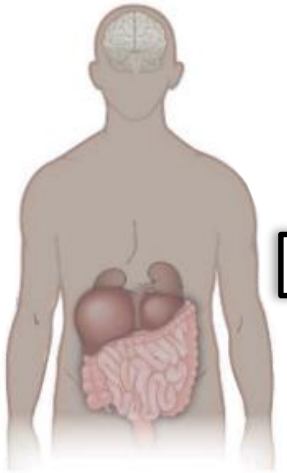
Matrigel®

In collaboration with Hans Clevers lab, Utrecht

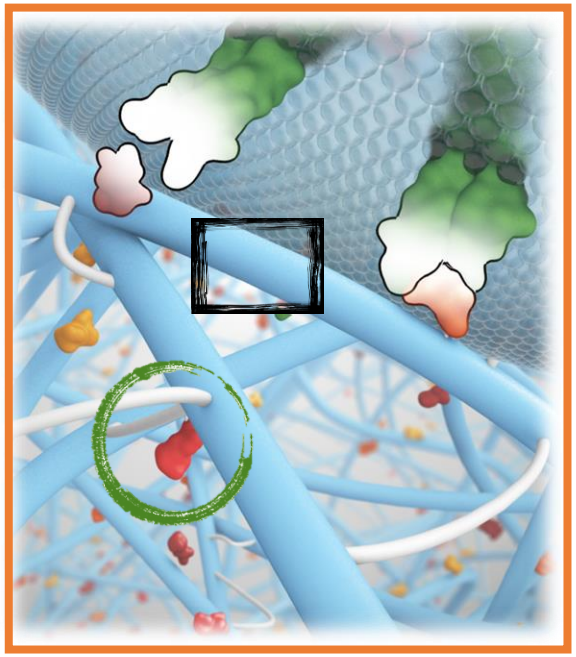
Conclusion: Bioinspired fibers as artificial functional scaffolds for organoid expansion

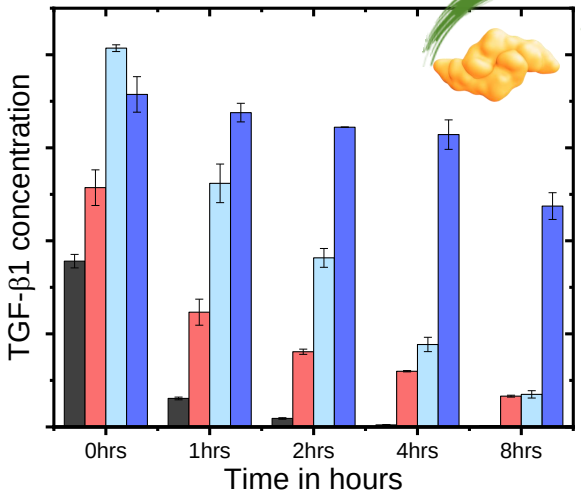


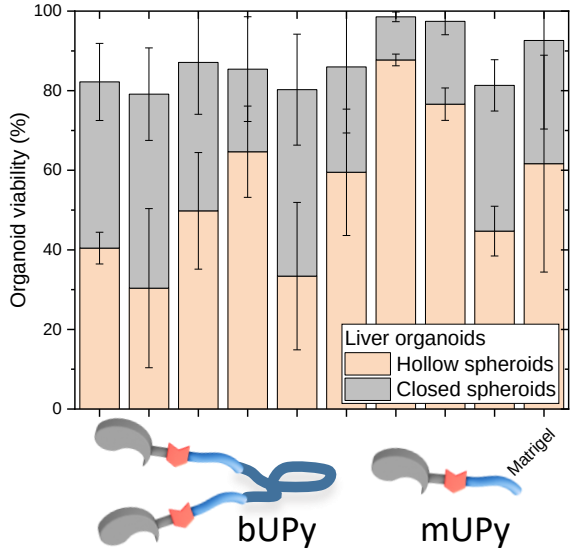
Versus



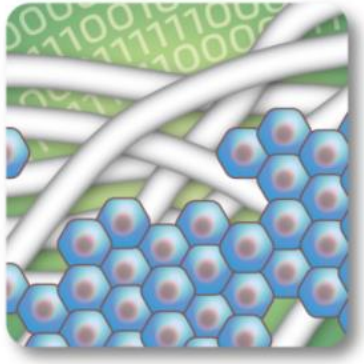
Organ regeneration?



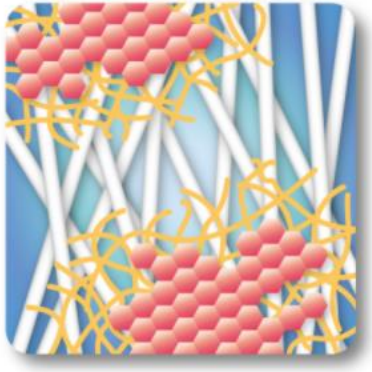




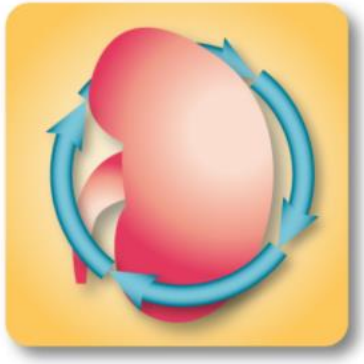
Outlook: research will be continued as part of MDR and REGMEDXB programs



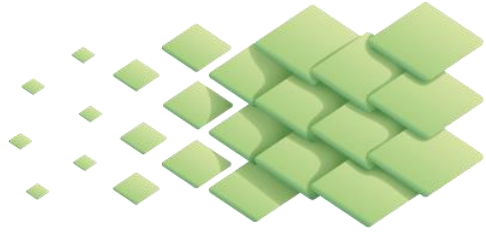
Materials, cells and organoids



Materials-driven in situ tissue regeneration



Regeneration of complex organ functions



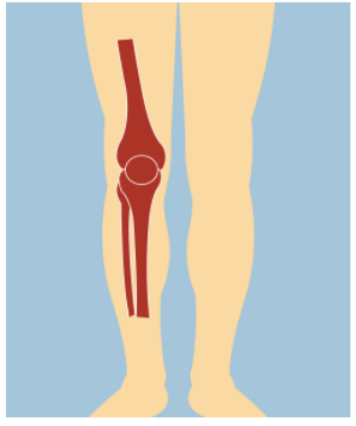
materials-driven regeneration

REGMEDXB

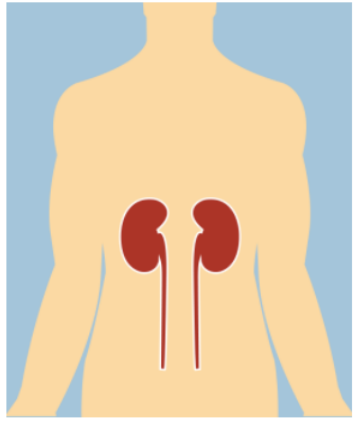
REGENERATIVE MEDICINE CROSSING BORDERS

Phase 1 of RegMed XB begins with four projects

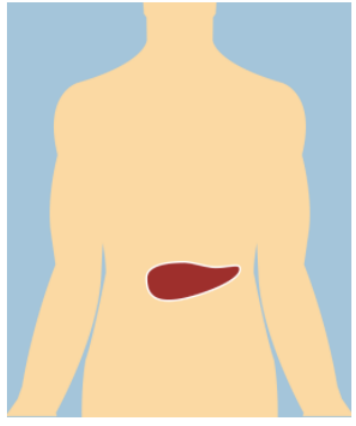
With partners from academia, industry, health foundations, and regional governments, RegMed XB has already funded three projects for five years.



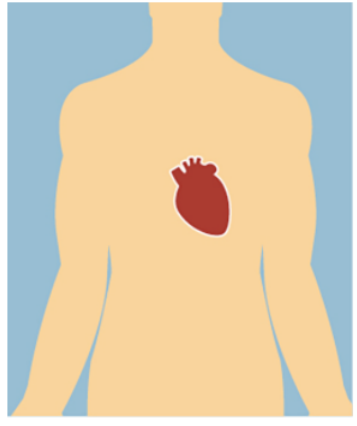
Taking steps towards a bioengineered joint.



A first subunit of a bioengineered kidney.



A proof-of-concept therapy for type 1 diabetes.



Regeneration of the human heart

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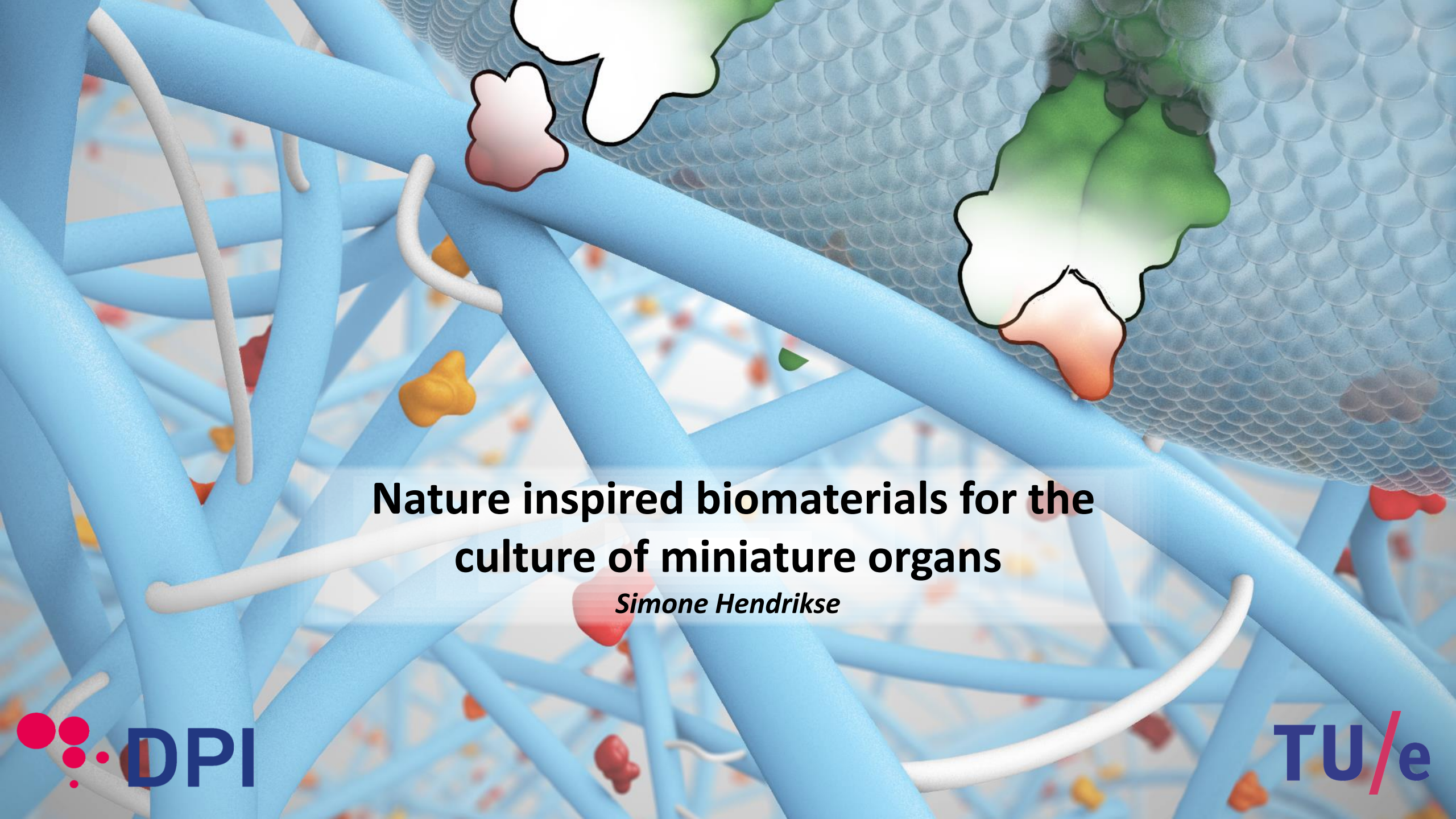

Nature inspired biomaterials for the culture of miniature organs

Simone Hendrikse

DPI

TU/e