

# Nanotecnologie e Insuline Smart

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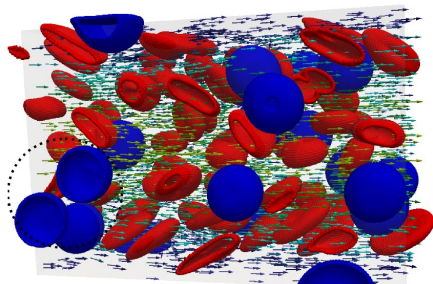
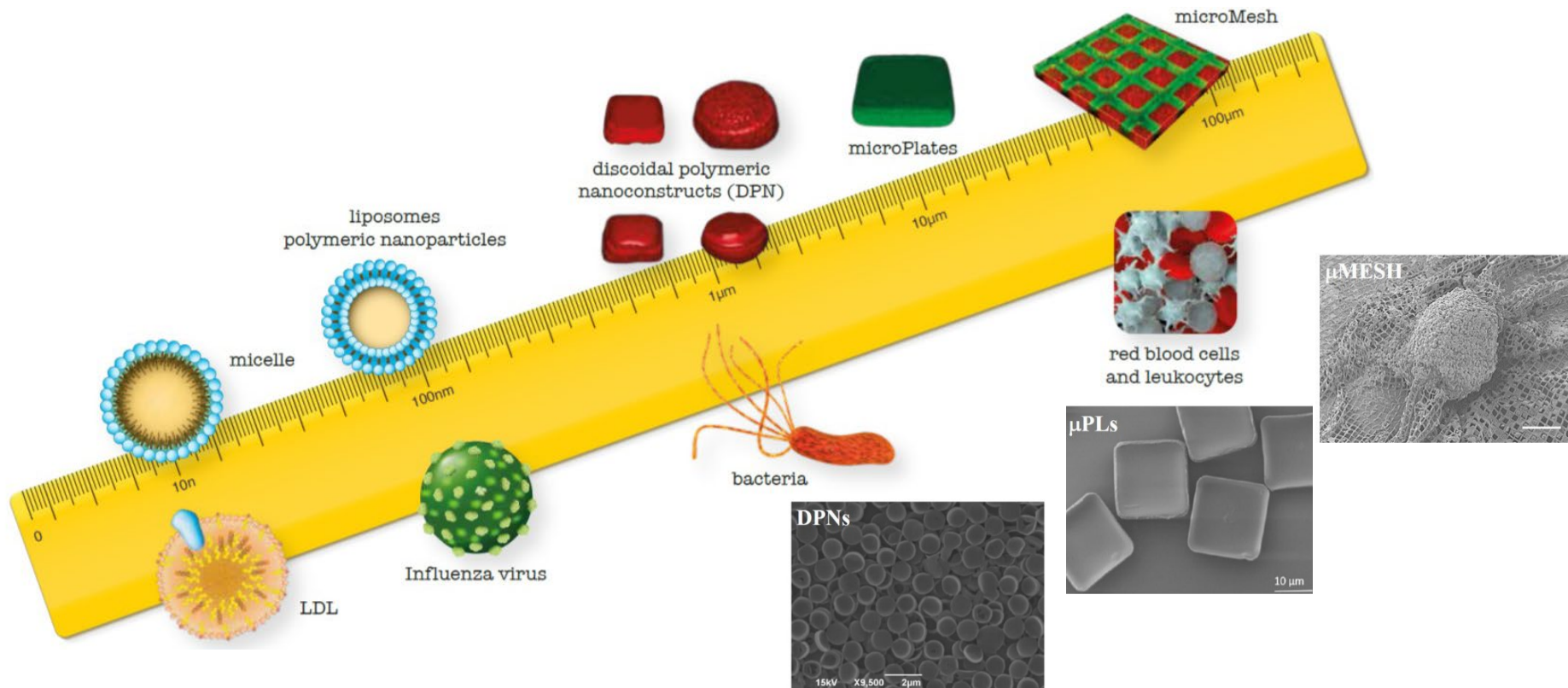
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<sup>2</sup> *San Martino Hospital, Genova, IT and*

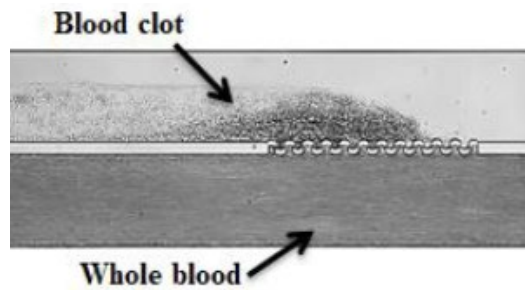
<sup>3</sup> *Stanford University, Palo Alto, CA,*



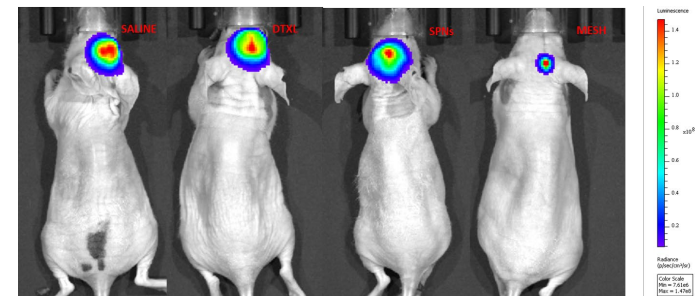
# Nanoparticles, Microparticles and Micromeshes



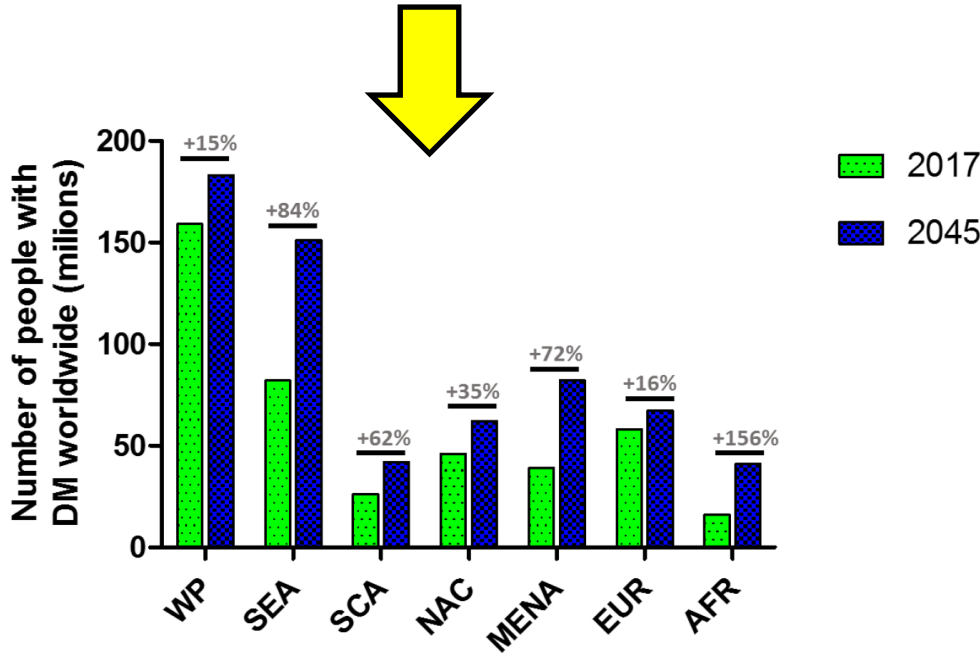
IN-SILICO 3D BLOOD FLOW



MICROFLUIDIC CHIP FOR BLOOD CLOTS



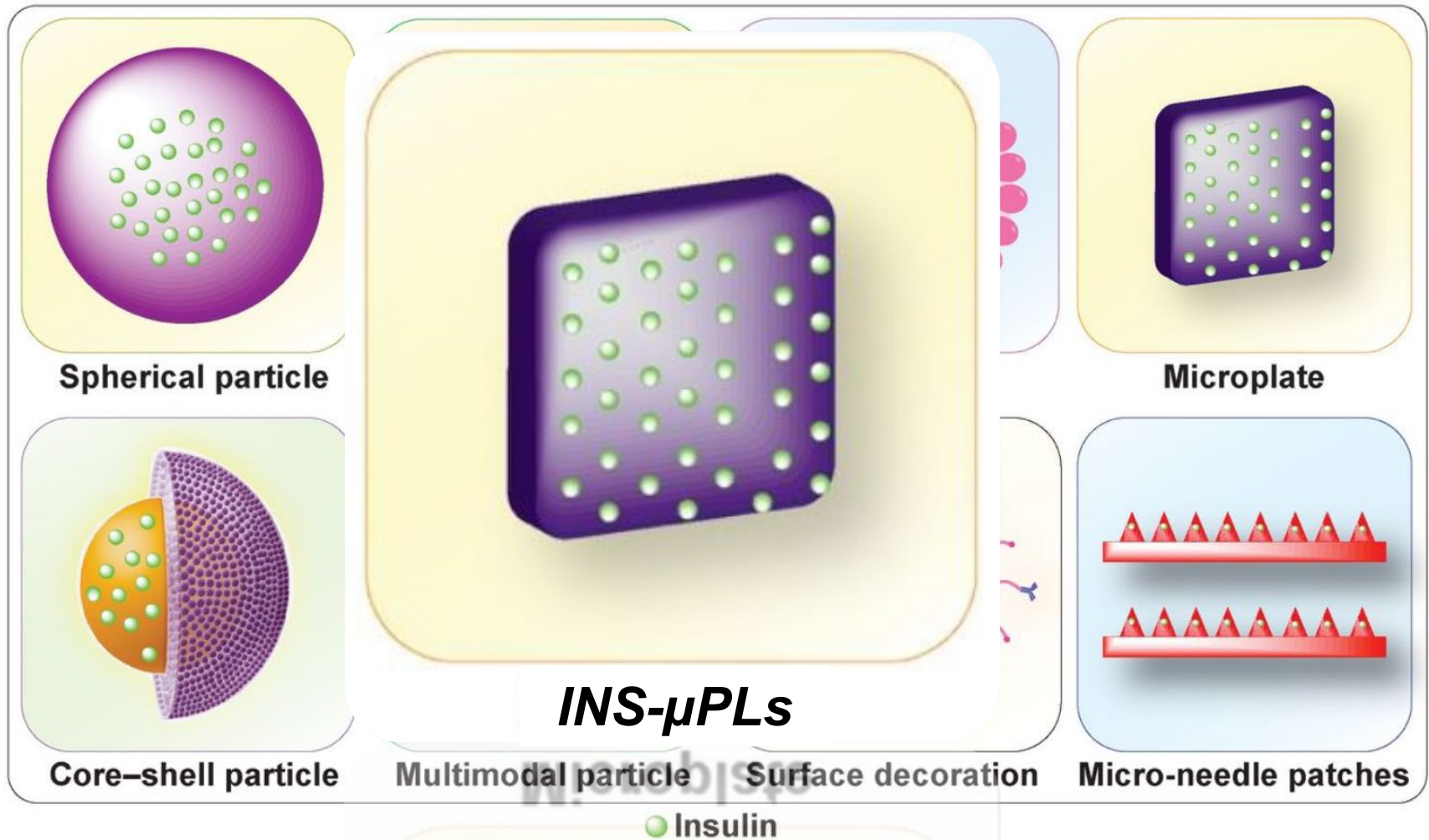
PRE-CLINICAL MODELS OF BRAIN TUMORS



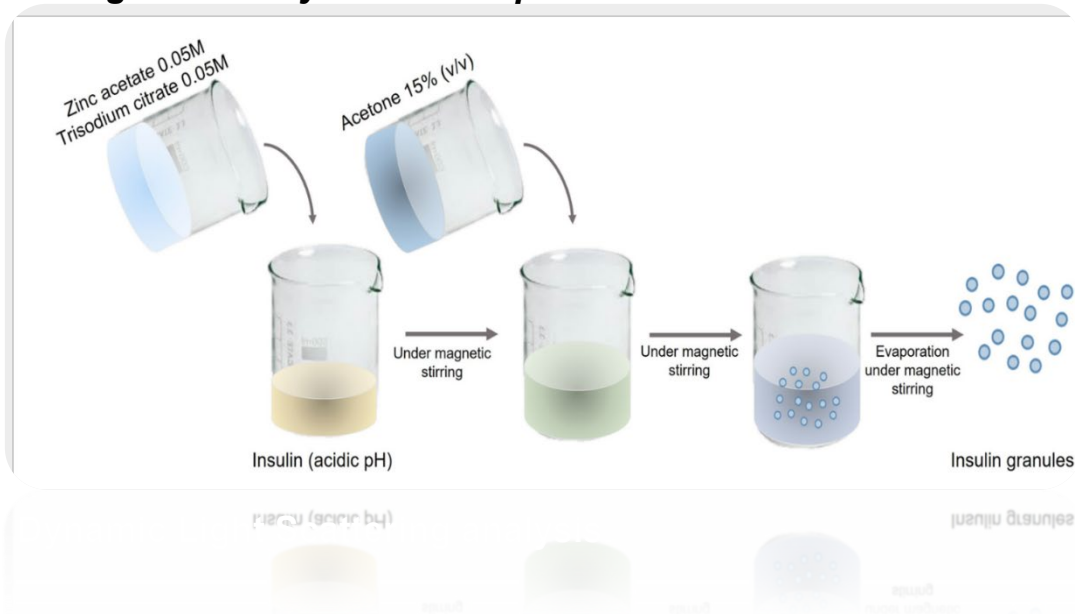
Number of people (millions) aged 20–79 years old with diabetes mellitus DM estimated by IDF, 2017 and 2045. (IDF = International Diabetes Federation, AFR = Africa, EUR = Europe, MENA = Middle East and North America, NAC = North America and Caribbean, SCA = South and Central America, SEA = South East Asia, WP = Western Pacific)

HEADACHY HUNGRY  
SWEATY CONFUSED  
SHAKY DIZZY  
GRUMPY

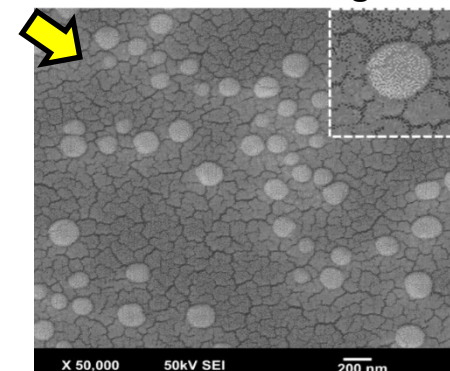
| Insulin Type                            | Onset   | Duration                |
|-----------------------------------------|---------|-------------------------|
| Short-acting Regular                    | 5–8 h   |                         |
| Intermediate-acting Insulin NPH         | 10–20 h |                         |
| Long-acting Insulin (Detemir, Glargine) | 1–2 h   | Relatively flat 14–24 h |



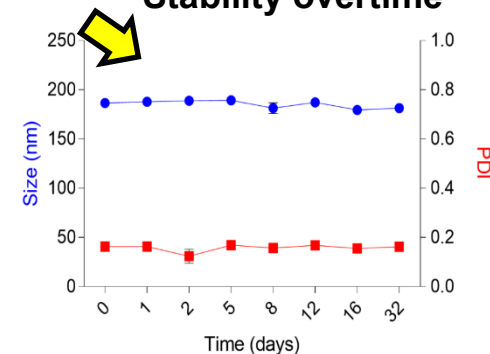
## INS-granules crystallization process



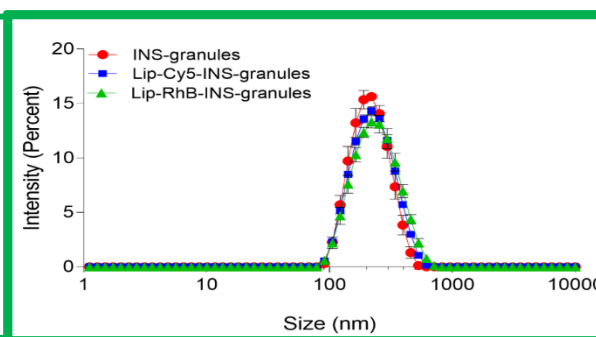
## HR-SEM image



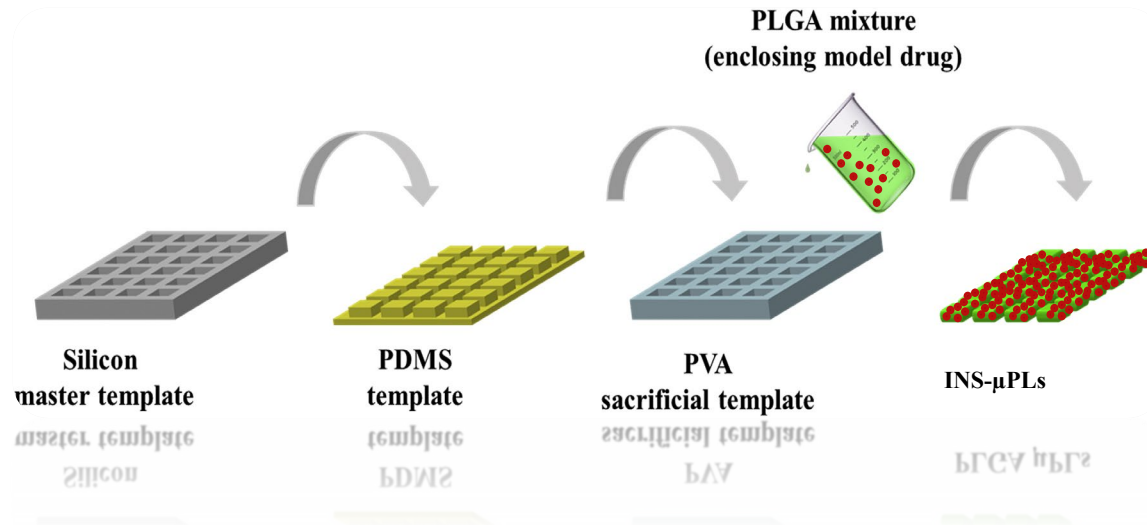
## Stability overtime



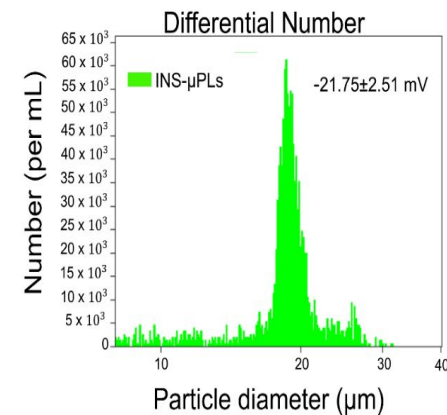
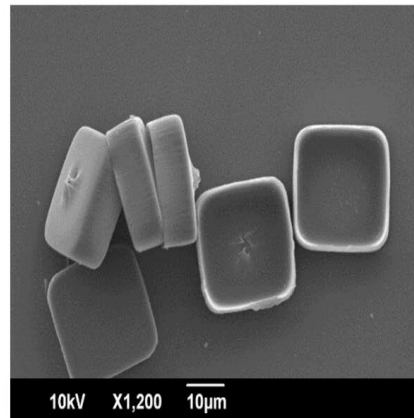
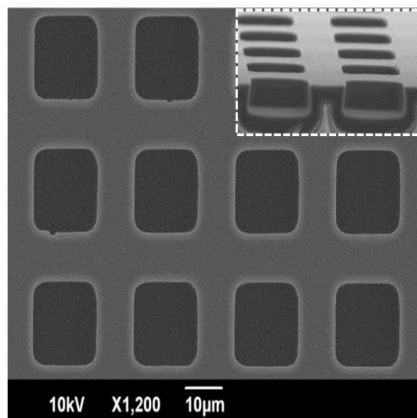
| Sample               | Size (nm)     | PDI         | Z-potential (mV) |
|----------------------|---------------|-------------|------------------|
| INS-granules         | 201.90 ± 3.12 | 0.10 ± 0.03 | -21.90 ± 1.65    |
| Lyp-Cy5-INS-granules | 189.20 ± 1.91 | 0.19 ± 0.01 | -18.40 ± 1.89    |
| Lyp-RhB-INS-granules | 219.10 ± 2.99 | 0.16 ± 0.02 | -15.20 ± 0.32    |



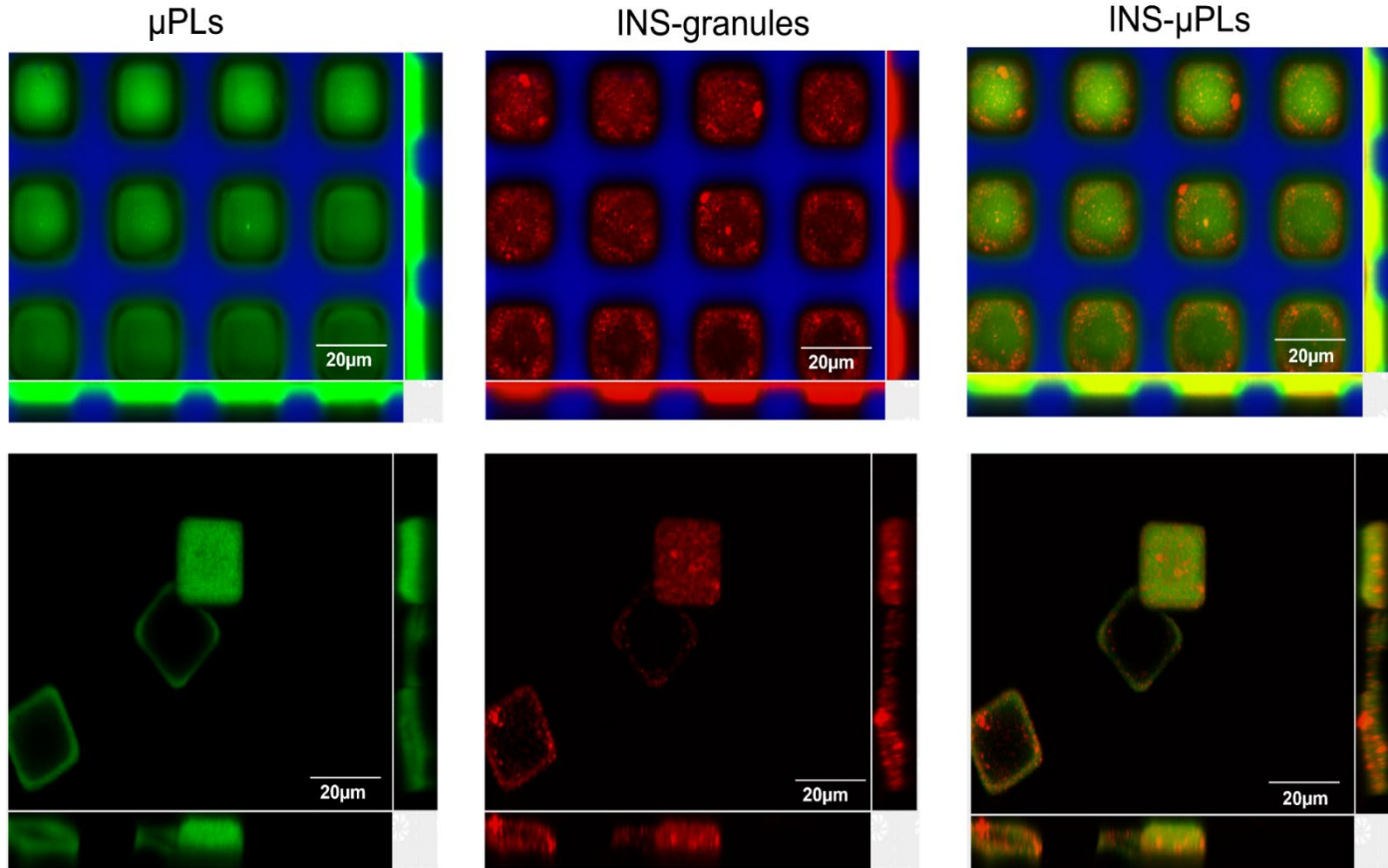
## INS- $\mu$ PLs fabrication process



## Physico-chemical characterization

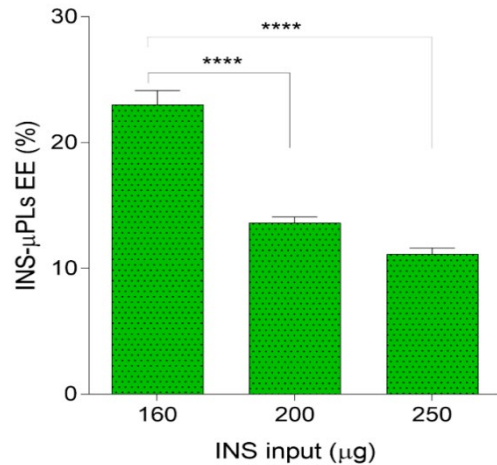


## *INS-granules distribution within $\mu$ PLs*

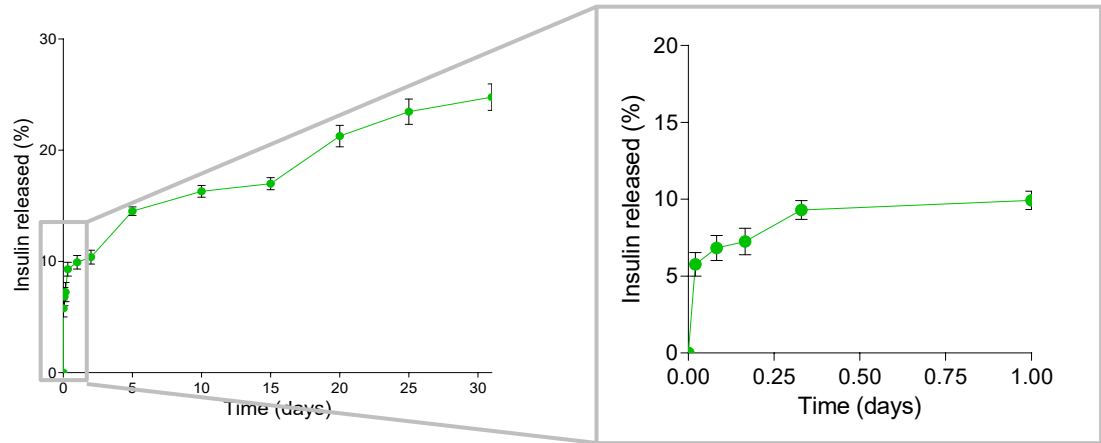


# Insulin granules loaded microPlates

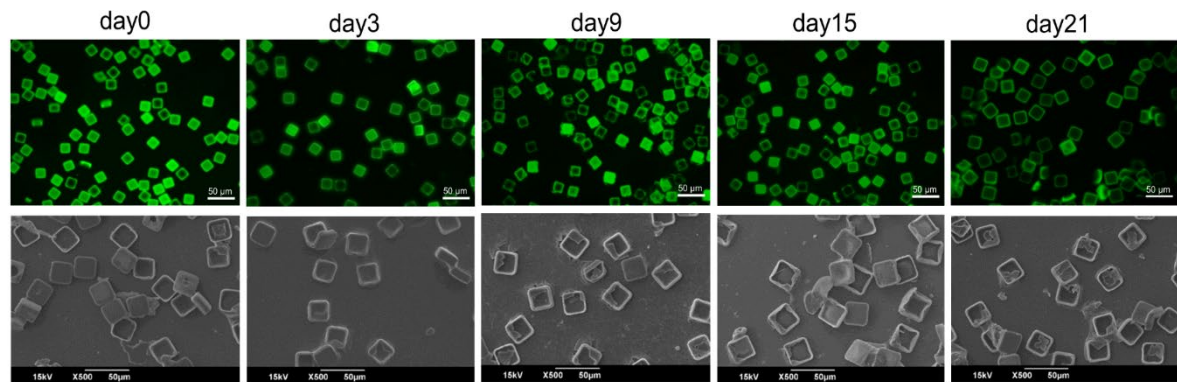
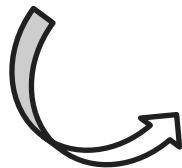
## Loading



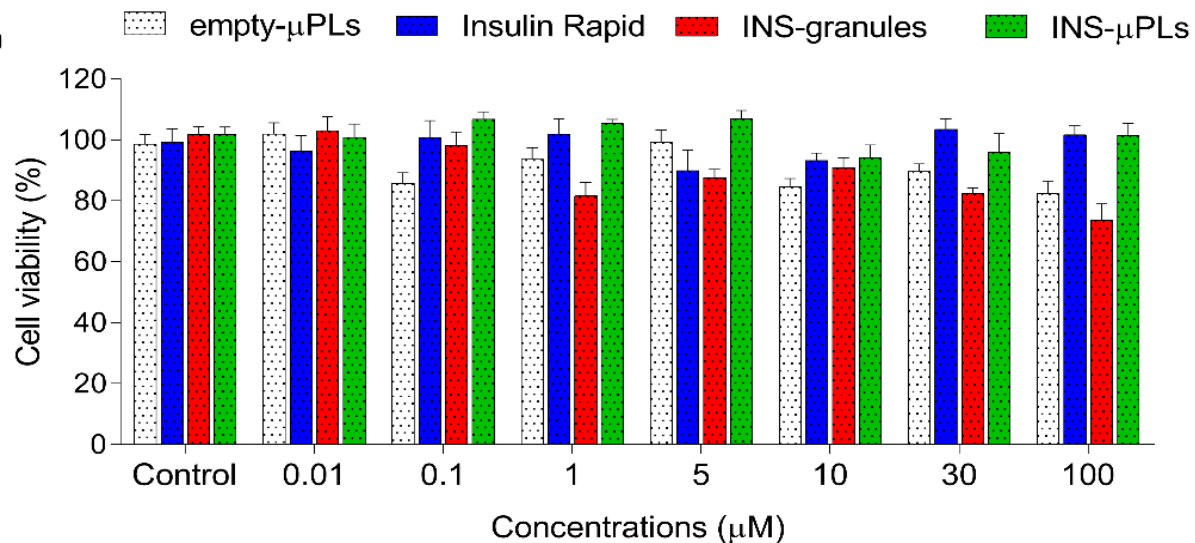
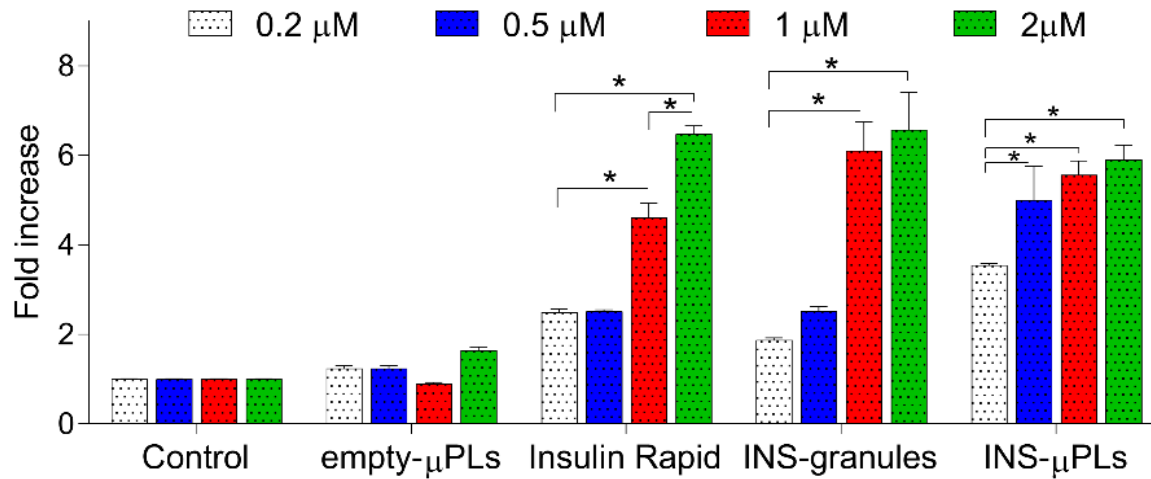
## Release profile



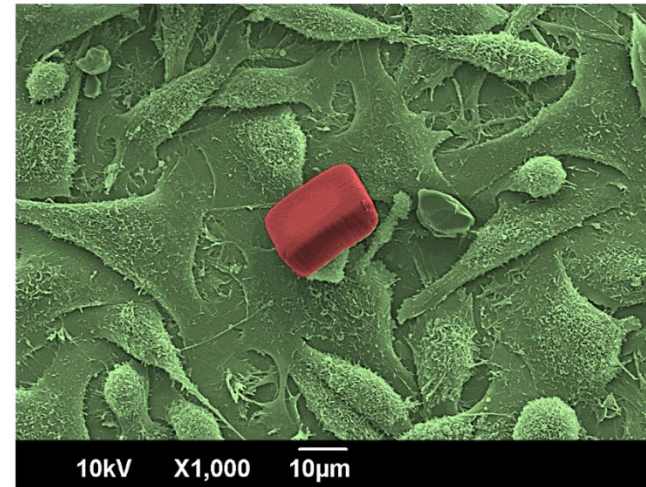
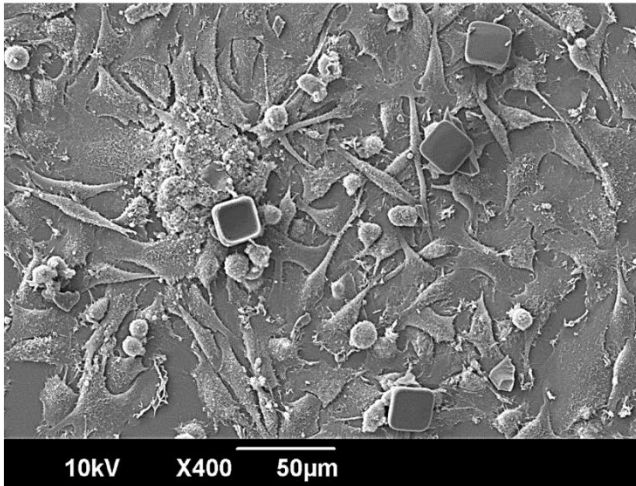
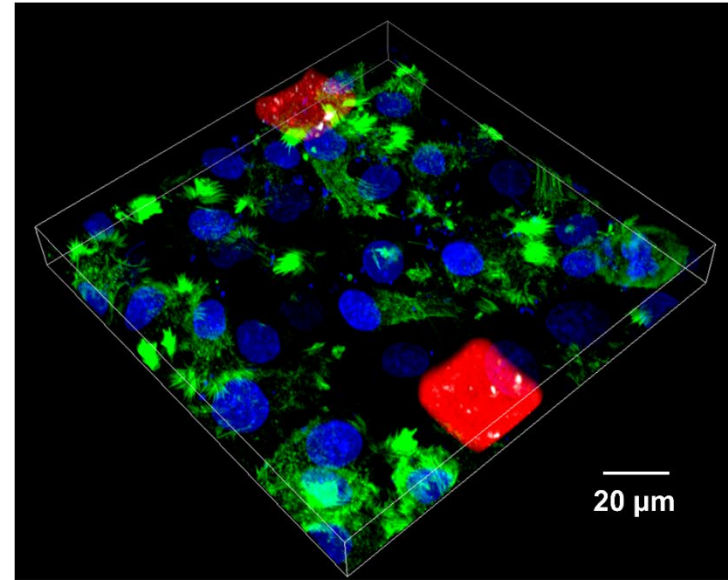
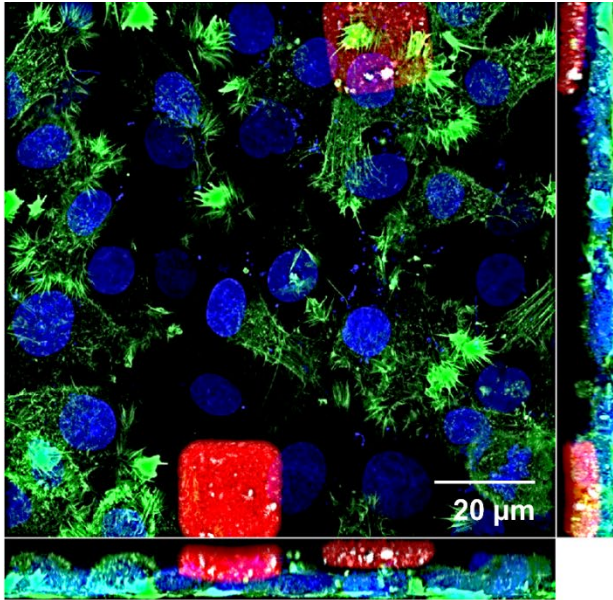
**Stability of particles  
over 21 days of incubation**



## Phospho-AKT @Ser473

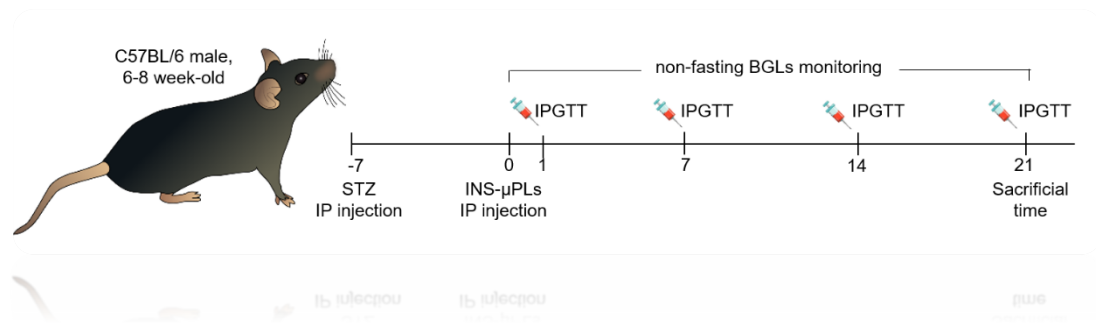


# Biological activity of INS- $\mu$ PL

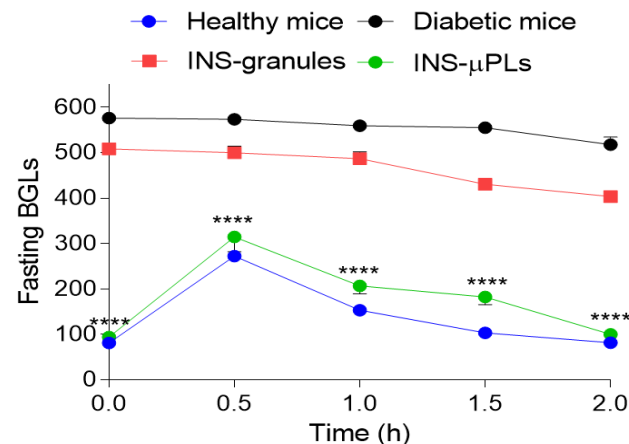


# *in vivo* evaluation of INS- $\mu$ PL

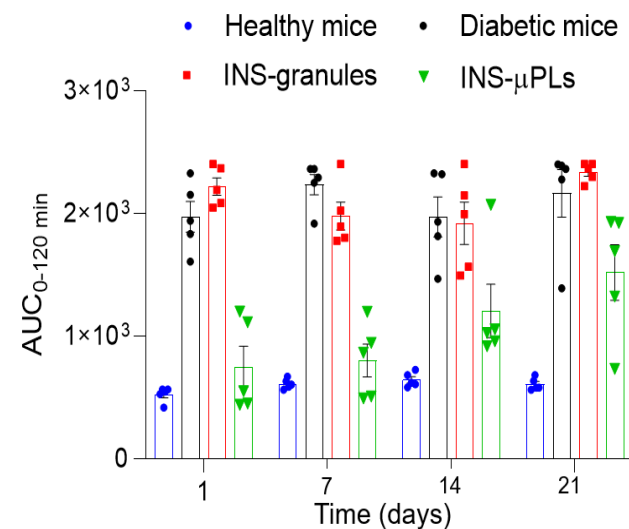
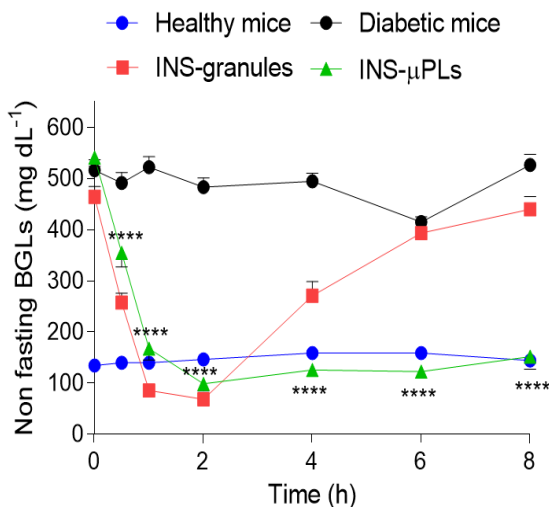
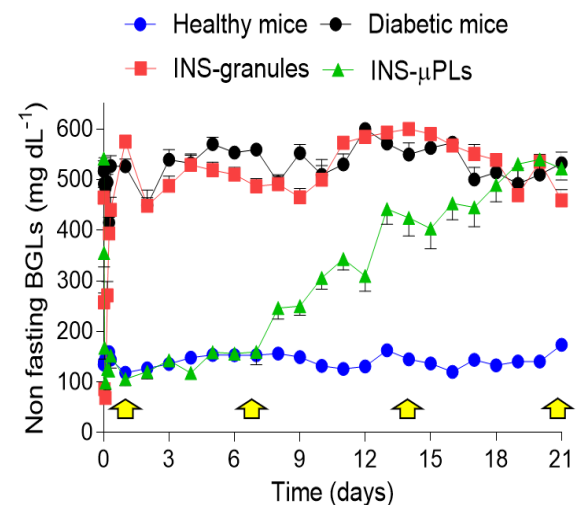
## Experimental set-up



## Intraperitoneal Glucose Tolerance Test



## Non-fasting blood glucose measurements



- ✓ Data generated to date show the potential of INS- $\mu$ PL as a promising platform for the treatment of T1DM with high and durable efficacy.
- ✓ Future studies will have to modulate the risk of hypoglycemia through the addition of a highly specific biochemical sensor to refine blood glucose level control

# Nanoparticles, Microparticles and Micromeshes



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