



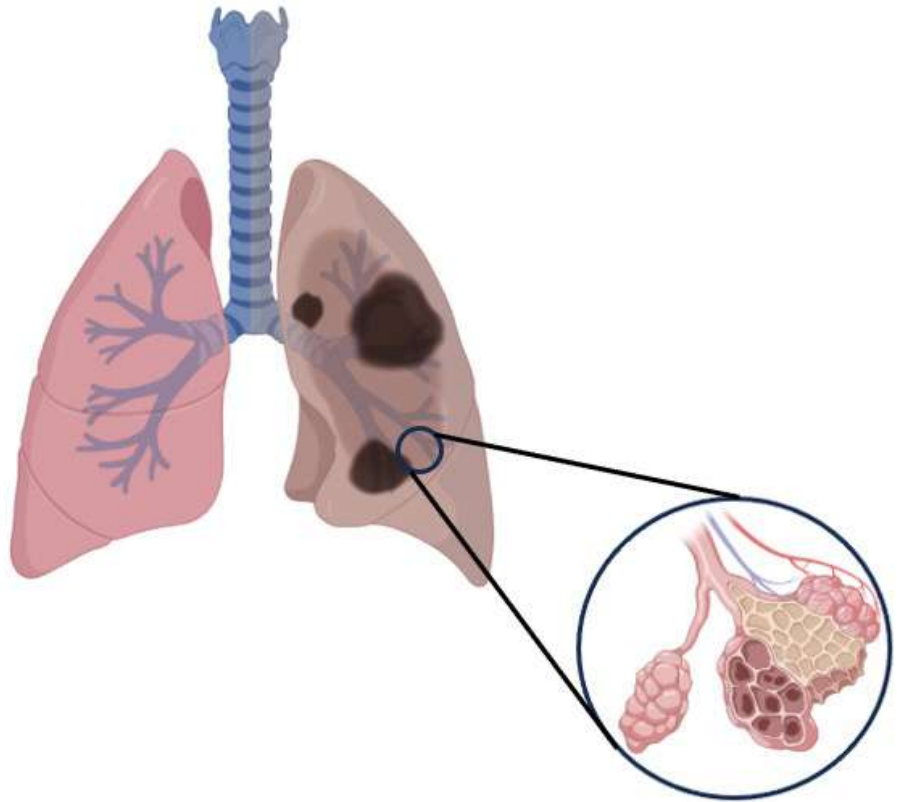
New inhalation drug delivery systems for the treatment of pulmonary fibrosis

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Project AIM

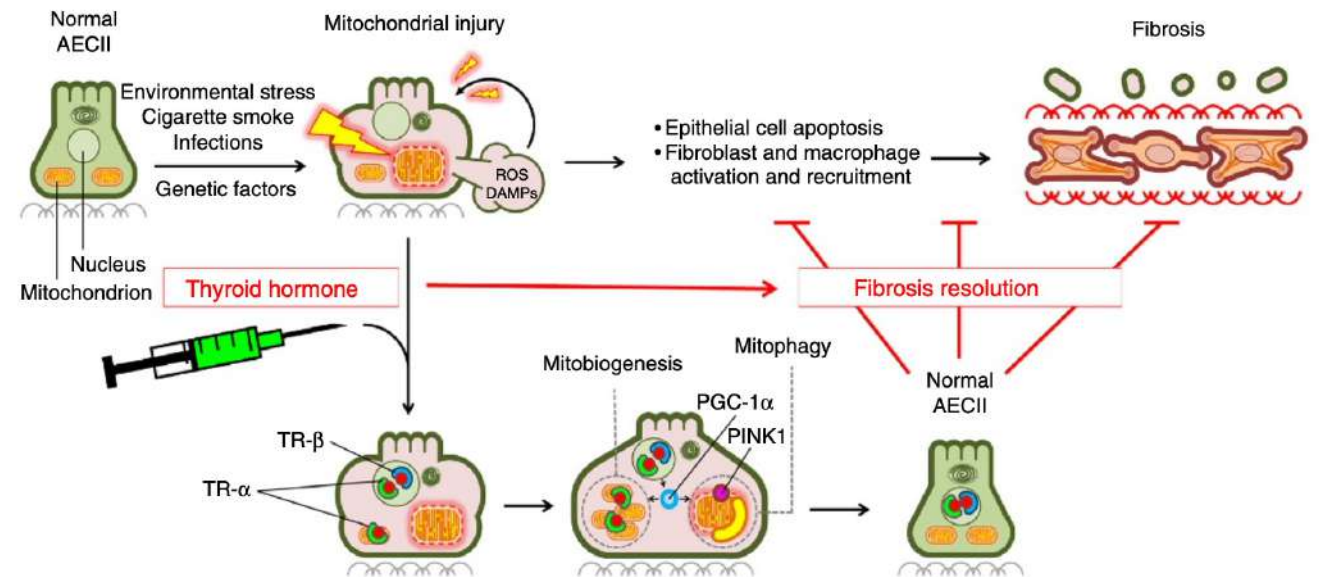


The aim of this project is the development of a novel treatment for the **lung fibrosis** based on a **levothyroxine** dry powder for inhalation.

nature
medicine

Thyroid hormone inhibits lung fibrosis in mice by improving epithelial mitochondrial function

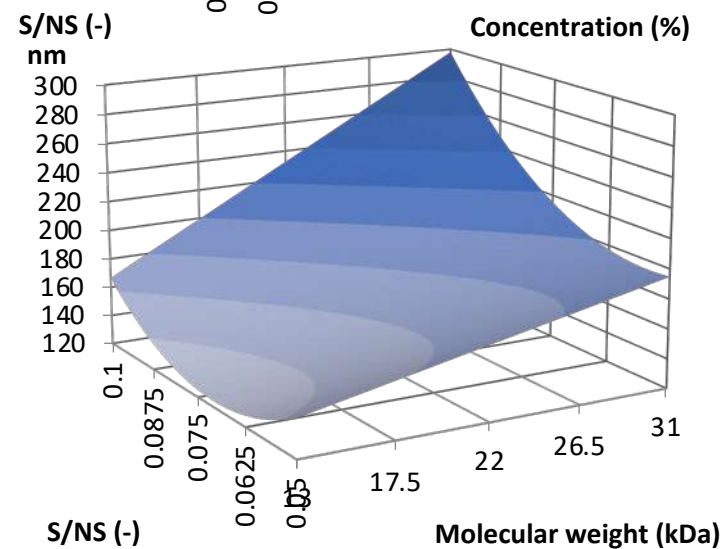
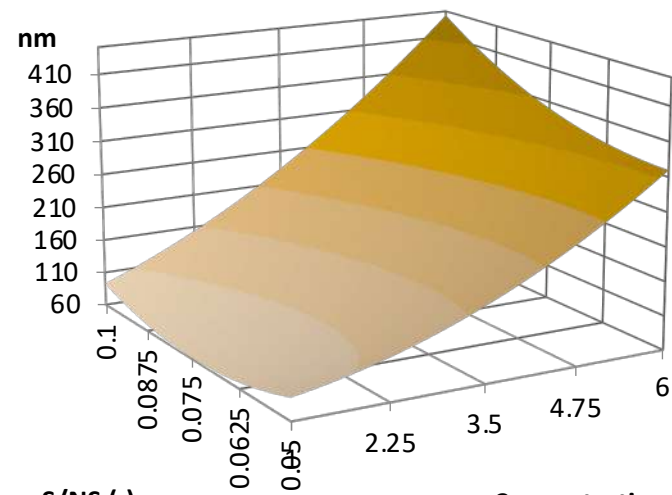
Guoying Yu^{1,11}, Argyris Tzouveleakis^{1,2,11}, Rong Wang^{1,10}, Jose D Herazo-Maya¹, Gabriel H Ibarra¹, Anup Srivastava¹, Joao Pedro Werneck de Castro^{3,4}, Giuseppe Delfulis¹, Farida Ahangari¹, Tony Woolard¹, Nachele Aurelien¹, Rafael Arrojo e Drigo⁵, Ye Gan¹, Morven Graham⁶, Xinran Liu⁶, Robert J Homer^{7,8}, Thomas S Scanlan⁹, Praveen Mannam¹, Patty J Lee¹, Erica L Herzog¹, Antonio C Bianco³ & Naftali Kaminski¹



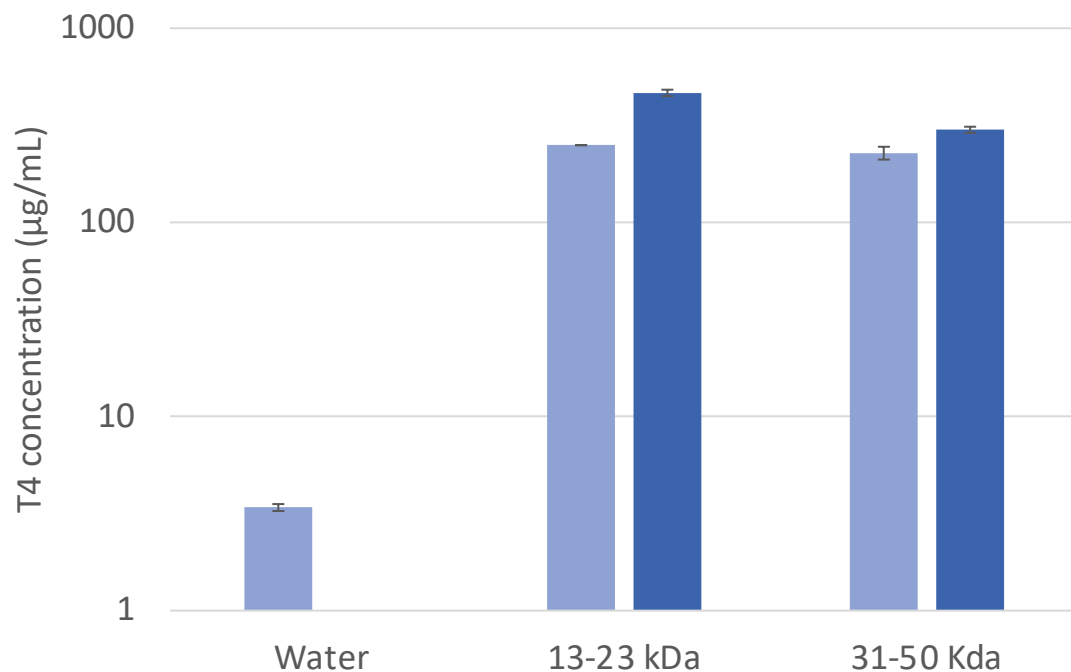
Yu G. et al. *Nat Med.* 2018;24(1):39-49.

PVA nanoparticles Production

	-1	0	1
Molecular weight (kDa)	13-28	-	31-50
Polymer concentration (%)	1	3.5	6
Solvent : antisolvent	1 : 10	1 : 15	1 : 20



T4 apparent solubility



Light blue: 1% w/v of PVA in water.
Blue: 3.5% w/v of PVA in water.

PVA Molecular weight (kDa)	PVA concentration (%)	Sample	T4 (% w/w)
13 - 23	1	S1	0.99
		S2	1.48
		S3	1.96
		S4	2.91
		S5	3.38

PVA-T4 powders

Sample	Size (nm)	PDI
S1	648.3	0.48
S2	636.3	0.48
S3	674.4	0.41
S4	917.3	0.65
S5	602.4	0.41

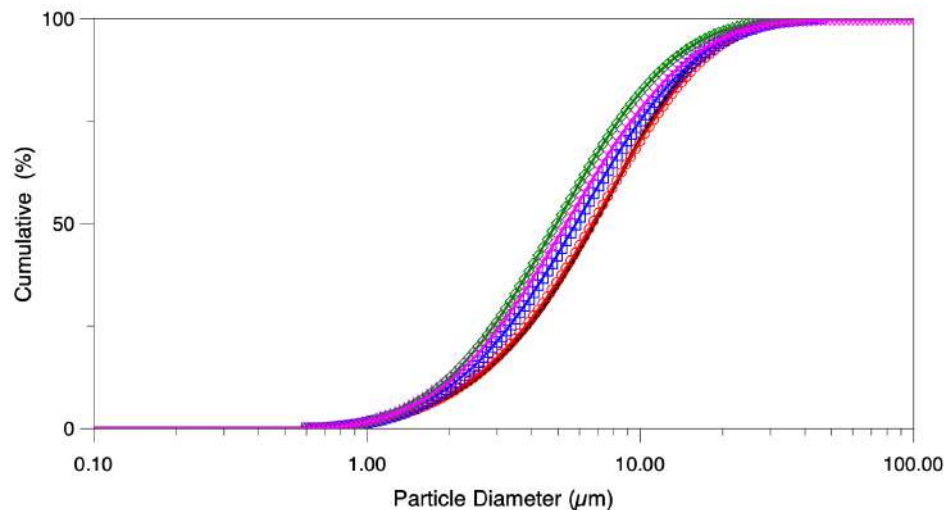
High pressure
Homogenization

Sample	Size (nm)	PDI
S1	422.7	0.29
S2	429.8	0.30
S3	436.3	0.25
S4	481.7	0.33
S5	436.4	0.35

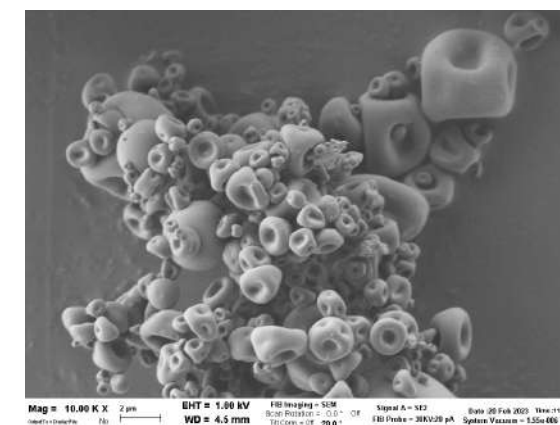
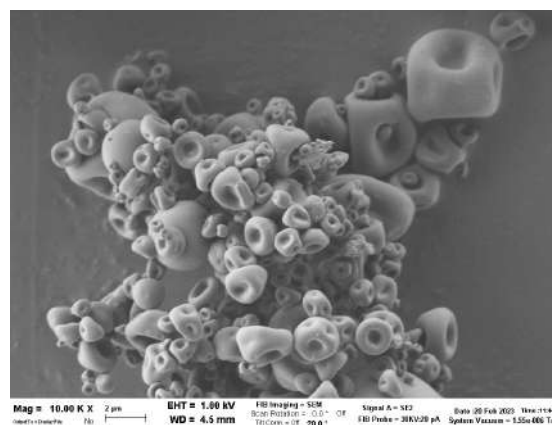
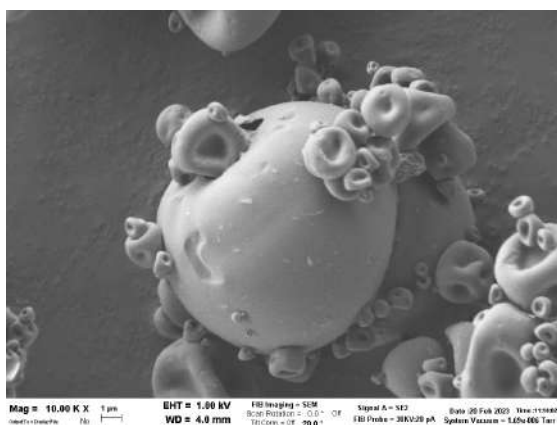
Drying



Powders characterization



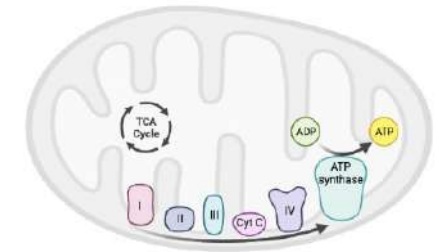
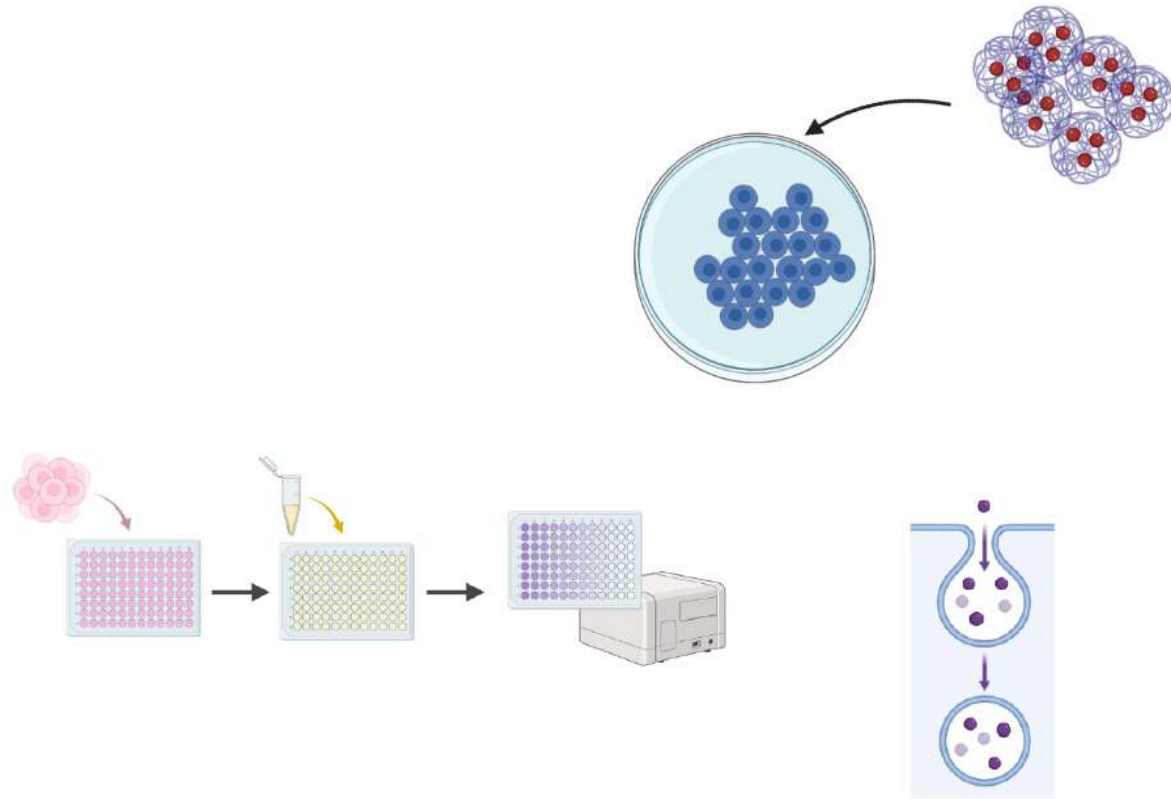
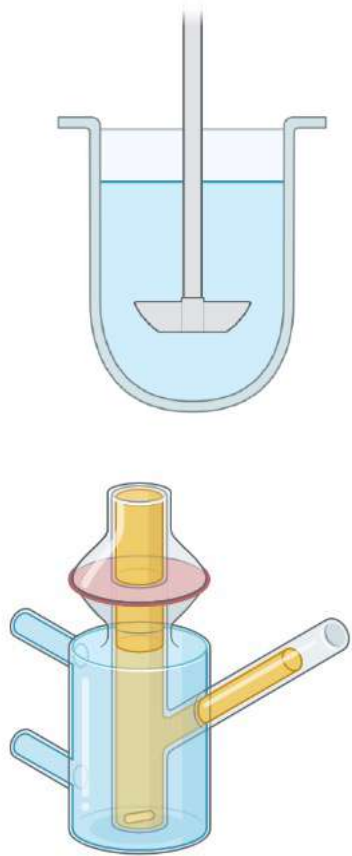
Sample	Emitted Dose (%)	Fine Particle Fraction (%)
S1	95.37	39.34
S2	97.05	51.94
S3	92.78	45.14
S4	94.41	41.87
S5	97.23	38.27



Conclusions

- PVA nanoparticles with a size and PDI suitable for intracellular delivery were obtained
- interaction between T4 and PVA exploited to obtain highly loaded nanoparticles
- Inhalable free flowing powders based on PVA-T4 were produced.
- The presence of aggregate could explain the high emitted dose and the low fine particle fraction

Ongoing activities



Images from biorender.com



Thank you for your attention

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