rPEGylation of Uricase for Reduced Immunogenicity

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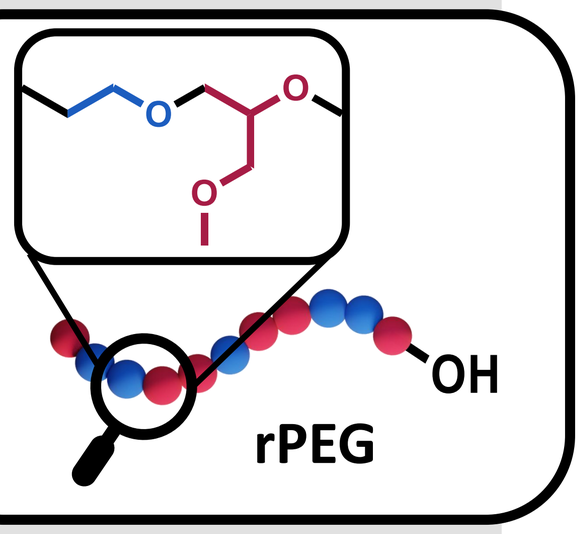
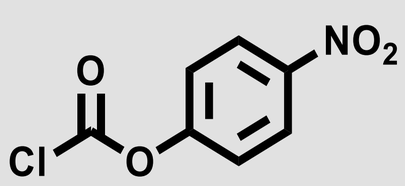
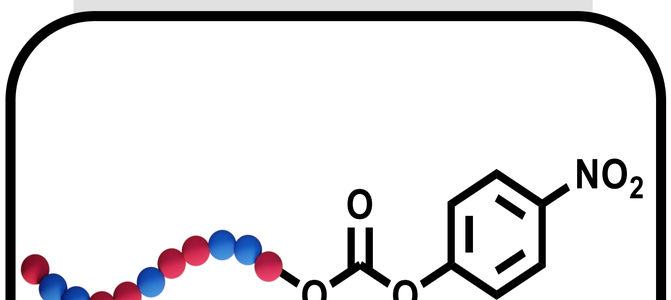
EO GME

Via
AROP

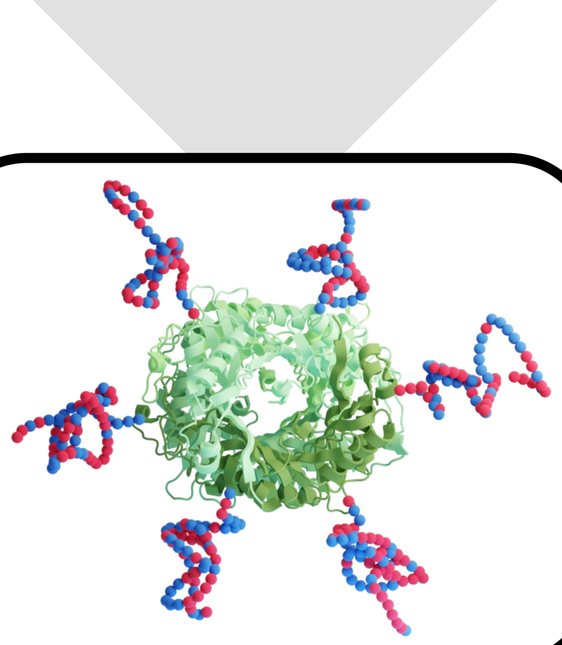


with



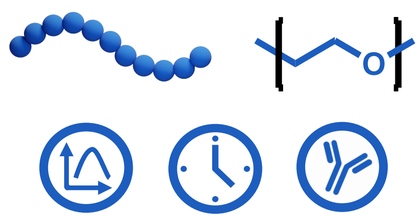


rPEGylation of Uricase



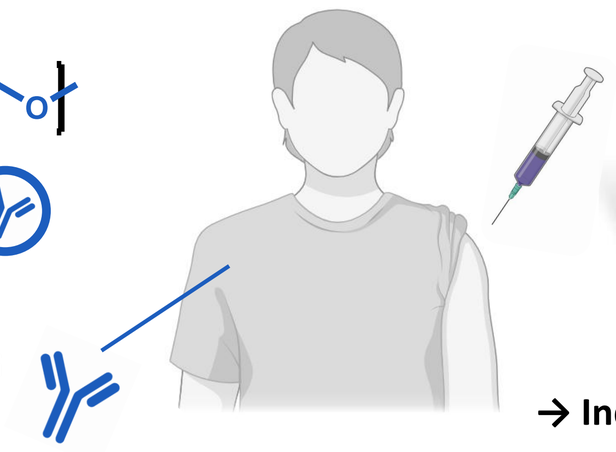
Introduction

PEGylation



Prevalence of Anti-PEG Antibodies (APAs)

→ Accelerated Blood Clearance (ABC)



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PEGylated Uricase

→ Induction of APAs

→ Immune Reactions (at High APA Titer)

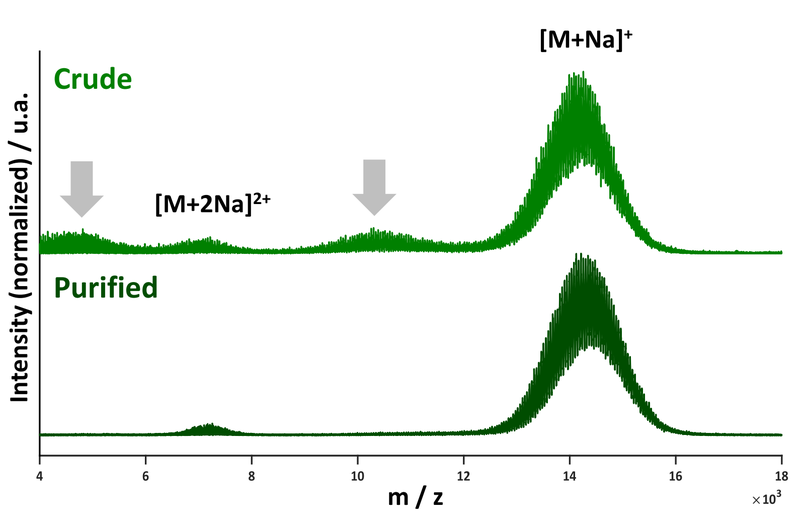
Synthesis

	M_p[a] (kDa)	GME[a,b] (mol%)	$Đ$[b]	$Đ_{HPLC}$[b]
$mPEG_{245}$	10.8	0	1.19	-
$rPEG_{218}^{0.50}$	14.4	50	1.22	1.08

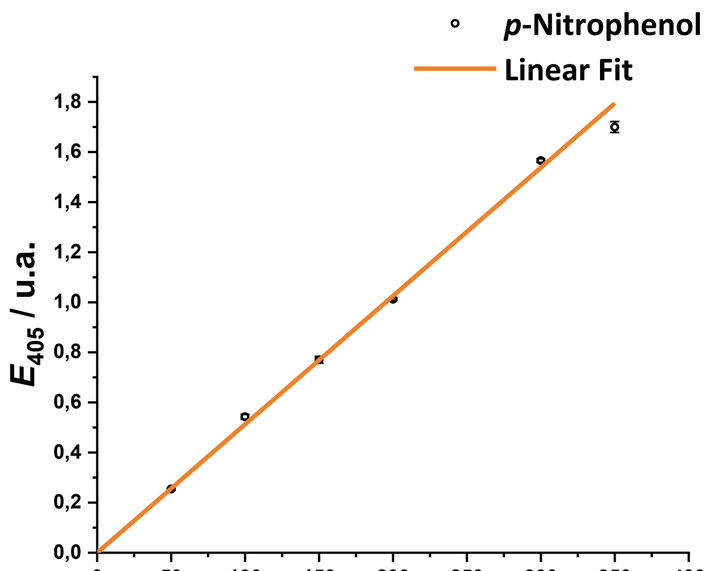
[a] Determined via MALDI-ToF (Matrix: DCTB, KTFA)
[b] Determined via SEC (Eluent: DMF, Standard: PEG)

Randomized Copolymerisation of GME and EO results in rPEG.

Purification via HPLC:



Activation



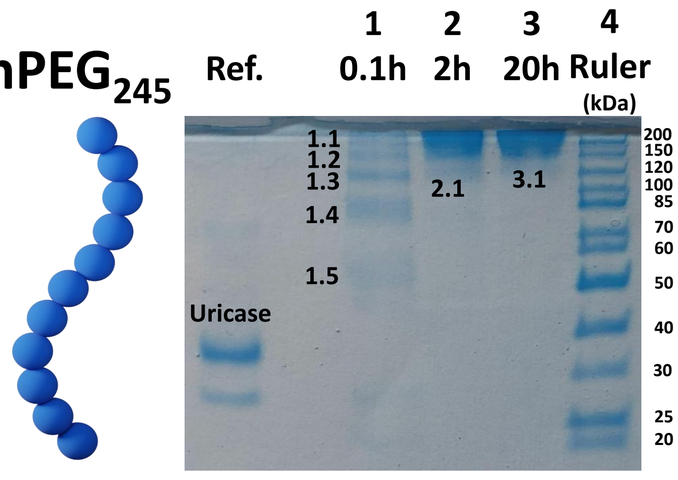
Degree of Activation α can be quantified via UV-Vis Spectroscopy

	Eq. NPCF	α (%)
$mPEG_{245}$-NPC	2.2	Quant.
$rPEG_{218}^{0.50}$-NPC	2.0	88

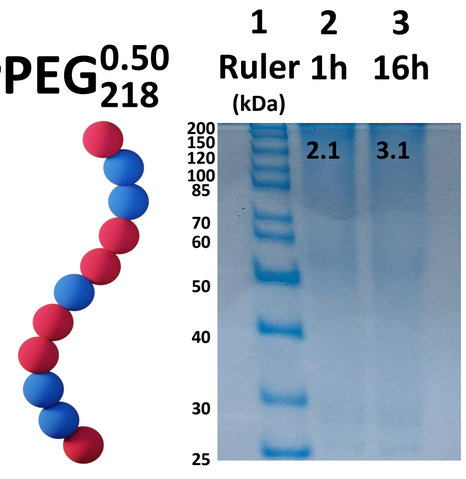
NPC Activation of rPEG is Analogously to mPEG Accessible.

Conjugation

$mPEG_{245}$



$rPEG_{218}^{0.50}$



First rPEGylation of Uricase was Successfully Performed.

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