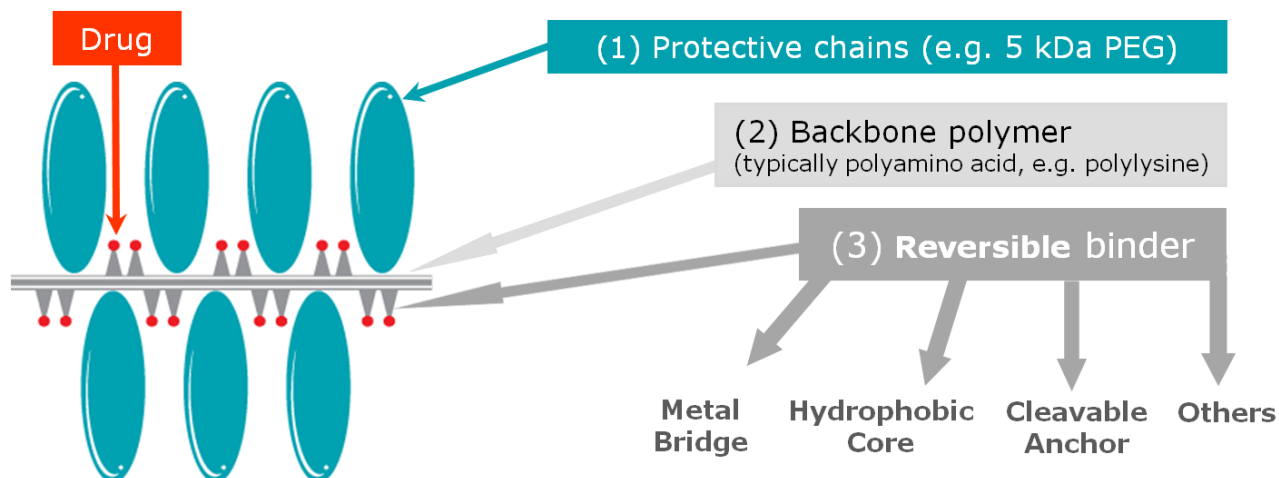


Broadly applicable nanocarrier (~20 nm) for enabling and improving protein and peptide therapeutics



## Description

- Entire complex has half-life of 20-60 hrs, controlled by design
- Reversible binder creates a high affinity, non-covalent interaction with the drug
- Multiple reversible binding chemistries add broad applicability
- PGC is ideal for passive accumulation in tumors, infection, and inflammation: diameter ~20 nm and MW ~350 kDa

## Advantages

The PGC molecule and the API will non-covalently combine during formulation and result in:

- Extended and controlled drug half-life
- Improvement of the API water solubility
- Reduced risk of aggregation
- Targeted accumulation in solid tumors, inflamed and infected tissues enabled through the PGC-API size

## Action

The PGC molecule acts as an excipient with no modification of the drug molecule. The PGC molecule is fully biodegradable and biocompatible, reversibly binding the drug molecule. The PGC binding mechanism can be tailored to the specific API molecule.

## Technological Superiority

The PGC platform provides significant advantages in comparison to PEGylation, fattylation, glycosylation, HESylation, polymer conjugation, or changes in the API's primary structure, for example.

## Routes of Delivery for PGC-API

Tested: IV, SC, and IM; others are feasible.

## IP position

The PGC technology has strong patent protection based on more than 10 recently issued or pending patent families.

## The PGC process

Fast and cost effective.

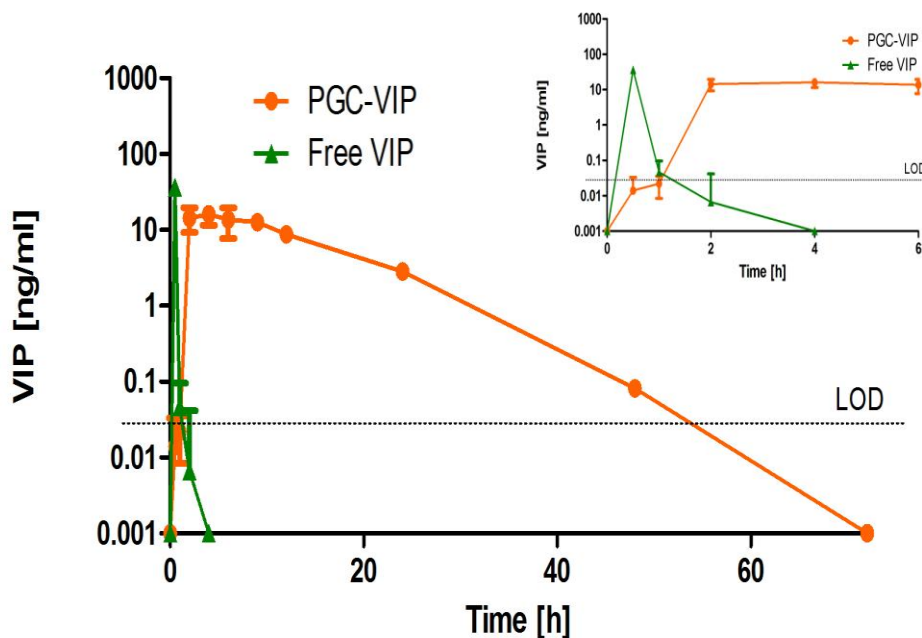
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## PGC Compared to No carrier, HESylation / PEGylation and Liposomes / Micelles

PGC superiority over No Carrier	PGC superiority over HESylation & PEGylation	PGC superiority over Liposomes & Micelles
<ul style="list-style-type: none"> <li>Extends circulation</li> <li>Accumulates in infected, inflamed and tumor tissues</li> <li>Mitigates non-specific interactions</li> <li>Protects from enzymatic and hydrolytic degradation</li> <li>Improves solubility</li> </ul>	<ul style="list-style-type: none"> <li>No modification of API</li> <li>Protection from reactions at SC injection site</li> <li>Smaller Mw PEG in PGC are safer</li> <li>No loss of activity</li> </ul>	<ul style="list-style-type: none"> <li>PGC is a discrete molecule, not a complex</li> <li>From SC injection, PGC-API traffics to the bloodstream intact</li> <li>Deeper distribution into infected, inflamed and tumor tissues</li> <li>PGC-API complex is much less dilution dependent</li> </ul>

### Pharmacokinetics Example: Vasoactive intestinal peptide (28 amino acids, unformulated half-life ~2 minutes)

- Subcutaneous PK of VIP in mice illustrates PGC's ability to extend serum half-life.
- (inset) Early time points: Note the lack of a "burst" effect with PGC.



### Product Examples (pre-clinical stage)

Product	Indication	Key Benefits of PGC Formulation
PGC VIP (peptide)	Rheumatoid Arthritis	Improved PK and MTD
PGC Basal Insulin (small protein)	Diabetes	1/day basal insulin, 505(b)2 regulatory path is feasible
PGC Anti-MRSA (27kDa protein)	MRSA infection	>100-times <i>in vivo</i> enhancement of bacterial killing and 10-times improvement in residence time
Undisclosed Large Protein	Undisclosed	Improved PK, 505(b)2 regulatory path is feasible