

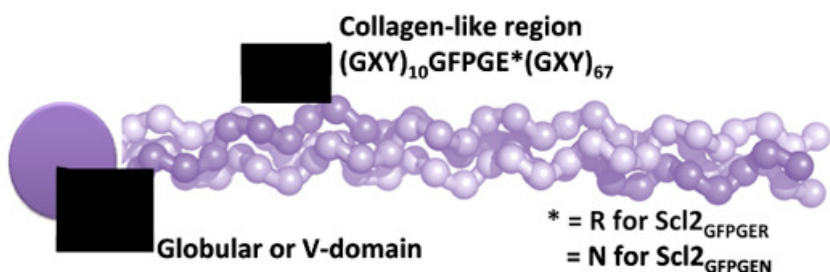
"Designer Collagens"

"Designer Collagens" are collagen-mimetic proteins originally derived from a group A *Streptococcus* protein, Scl2.28, initially discovered by Dr. Höök of Texas A&M Health Science Center and Dr. Lukomski of West Virginia University.¹⁻² Although the Scl2.28 protein contains the GXY repeats characteristic of collagen, it lacks hydroxyproline and does not require post-translational modification to attain a triple helical structure.³ These features enable facile recombinant expression in *E. coli*, circumventing concerns about the batch variability of native collagens as well as the high scale-up costs associated with solid-phase synthesis of collagen-derived peptides.¹⁻²

The parent "Designer Collagen" (DC1) was derived from the Scl2.28 sequence and lacks the array of cell adhesion, cytokine binding, and enzyme-cleavage sites associated with native collagen.⁴⁻⁵ DC1 therefore serves as a biological "blank slate" that only displays the selected receptor-binding sequences or enzyme-degradation sites programmed by site-directed mutagenesis. To date, ECM Technologies, a start-up founded by Dr. Magnus Höök, has generated two "daughter" DCs, DC2 and DC3, which incorporate $\alpha_1\beta_1$ and/or $\alpha_2\beta_1$ integrin-binding motifs based on the collagen sequences GF/LOGER⁶⁻⁷ (O; hydroxyproline). Specifically, DC2 binds both $\alpha_1\beta_1$ and $\alpha_2\beta_1$ integrins, whereas DC3 binds only $\alpha_1\beta_1$.⁸ These daughter proteins maintain the resistance to platelet aggregation associated with DC1⁸ while supporting cell-selective binding and appropriate integrin-mediated signaling.

Until recently, the use of DCs was limited to coatings due to their inability to self-assemble into stable 3D structures. However, DCs have now been successfully incorporated into 3D biomaterial platforms by coupling these proteins with established polymer chemistry to generate biosynthetic hydrogels based on functionalized DC and poly(ethylene glycol) diacrylate.⁹ Scl2.28-derived proteins have also been incorporated within 3D scaffolds via freeze-drying followed by glutaraldehyde crosslinking and have been shown to be cytocompatible and non-immunogenic in SJL/J and Arc mice.¹⁰ Given their unique properties, DCs represent a tailorable protein platform with strong potential utility in both fundamental and translational biomaterials research.

Figure



Designer Collagen Characteristics:

- Triple helix formation verified by circular dichroism.
- Melting temperature similar to mammalian collagen as measured by circular dichroism.
- Charged residues help stabilize the helix without hydroxyproline.
- The globular domain is required for refolding, but can be removed after helix formation.
- Can be readily modified by site-directed mutagenesis to contain specific cell adhesion or enzyme-degradation sites.
- Can be coupled with standard synthetic chemistry to form 3D scaffolds.

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