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# Supporting Information

## Design of biodegradable bi-compartmental microneedles for the stabilization and the controlled release of the labile molecule collagenase for skin healthcare

Concetta Di Natale [§ a,b], Domenico De Rosa [§ a], Martina Profeta [a], Rezvan Jamaledin [a], Alessandro Attanasio [a], Elena Lagreca [a], Pasqualina Liana Scognamiglio [a], Paolo Antonio Netti [a, b] and Raffaele Vecchione1 * [a].

[a] *Center for Advanced Biomaterials for HealthCare@CRIB, Istituto Italiano di Tecnologia, Largo Barsanti e Matteucci 53, Napoli 80125, Italy*

[b] *Interdisciplinary Research Center of Biomaterials, CRIB, University Federico II, P.le Tecchio 80, Naples 80125, Italy*

[§] *These authors contributd equally .*

* Correspondence should be addressed to Ing.PhD Raffaele Vecchione

E-mail: Raffaele.vecchione@iit.it

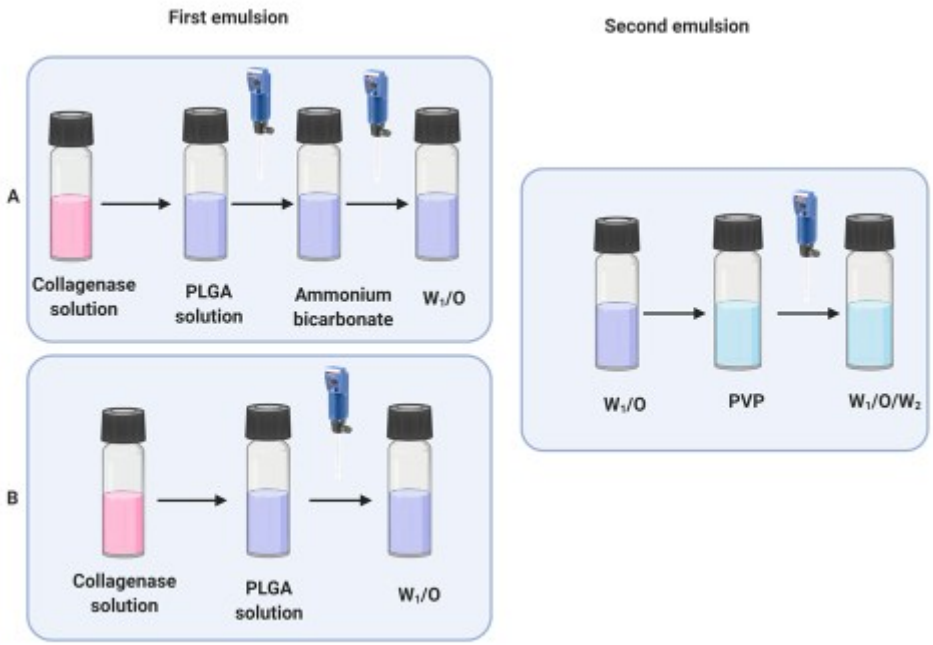


**Figure S1:** Collagenase MPs production with (A) and without (B) porogenic agent

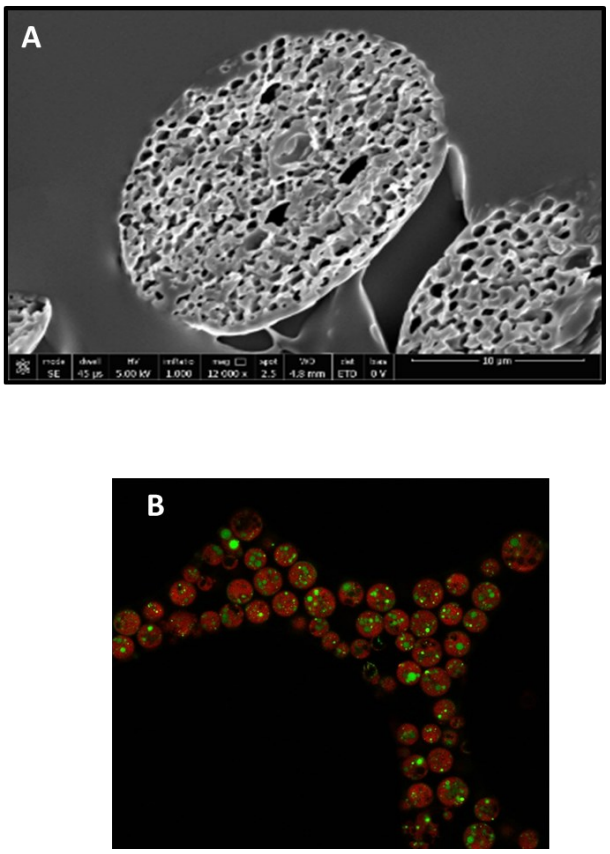


**Figure S2:** Morphological characterization of Collagenase-standard. A) SEM microscopy, B) Confocal analysis: Fluorescence images were acquired using a $\lambda_{exc}$ of 488 nm and a $\lambda_{emiss}$ between 500 and 600 nm. Red signal is related to PLGA acquired in DAPI range.

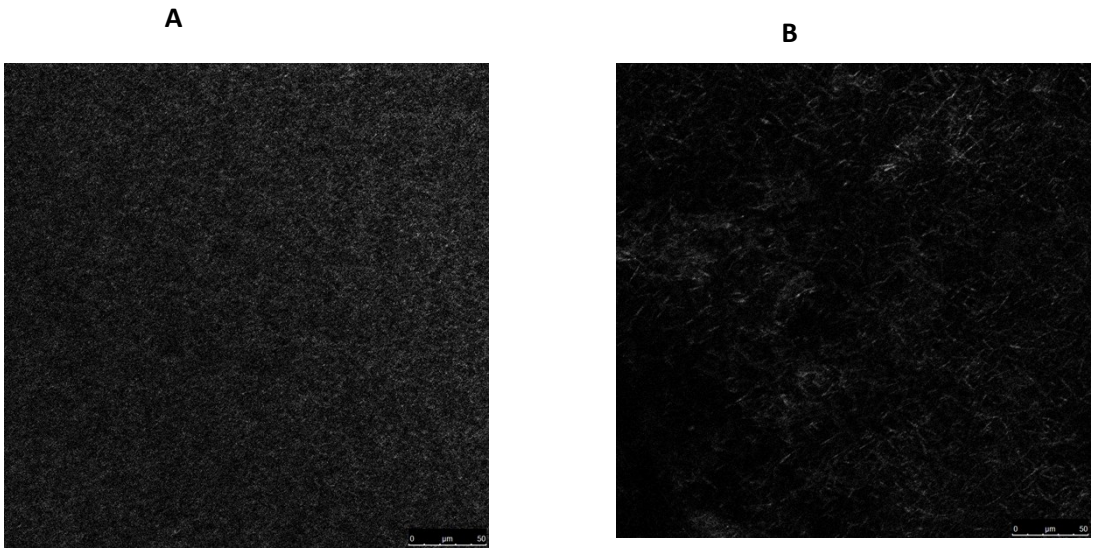

**Figure S3:** Z-stack analysis of A) control sample and B) treated collagen.

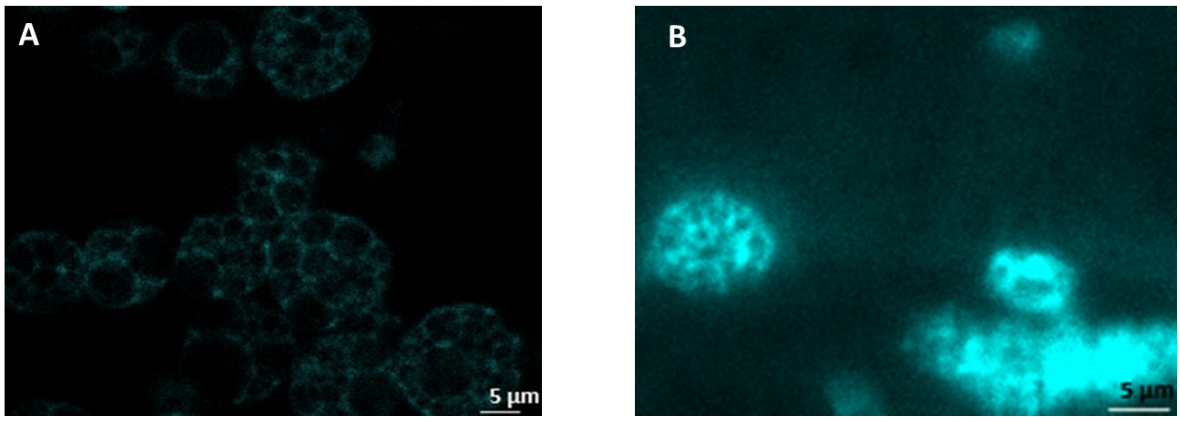


**Figure S4:** MPs before (A) and after microneedle production process (B).

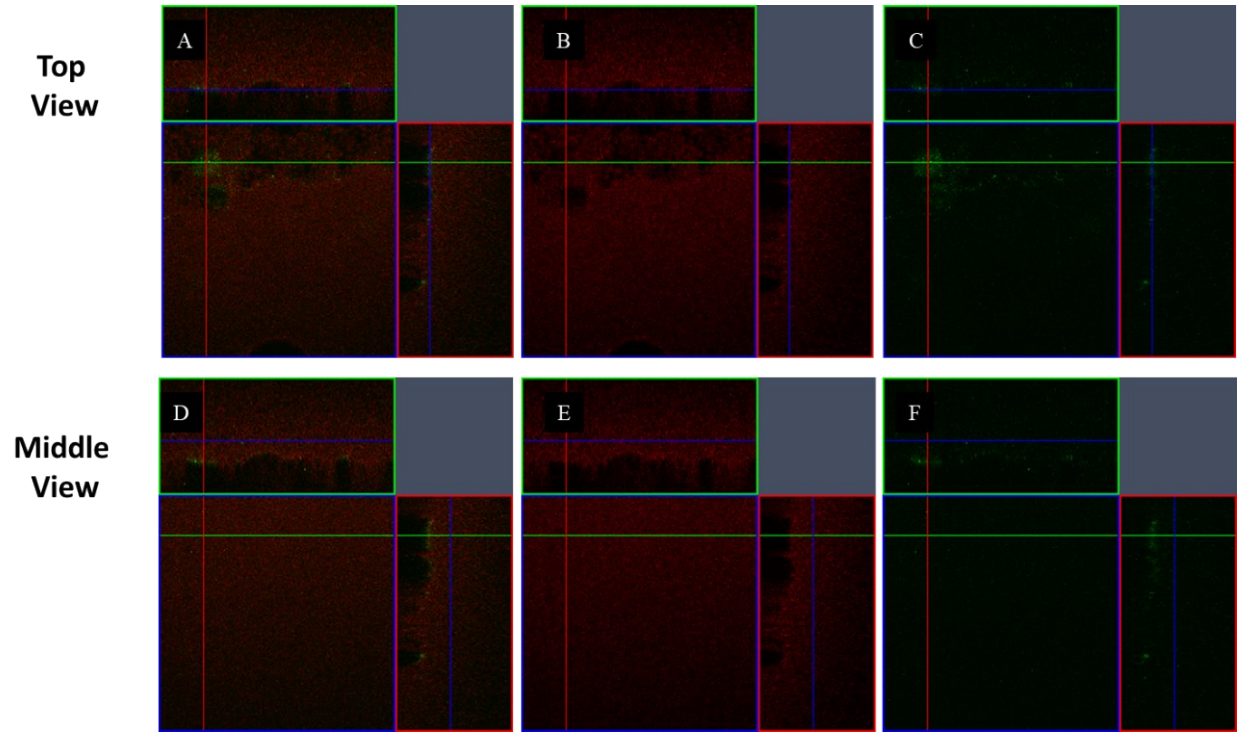

**Figure S5:** Release test of 600 µm microneedles loaded with the Standard MPs in the in vitro skin equivalent model after 30 min; top and middle view. A-D) Merge of green and red channels; B-E) red channel; C-F) green channel.

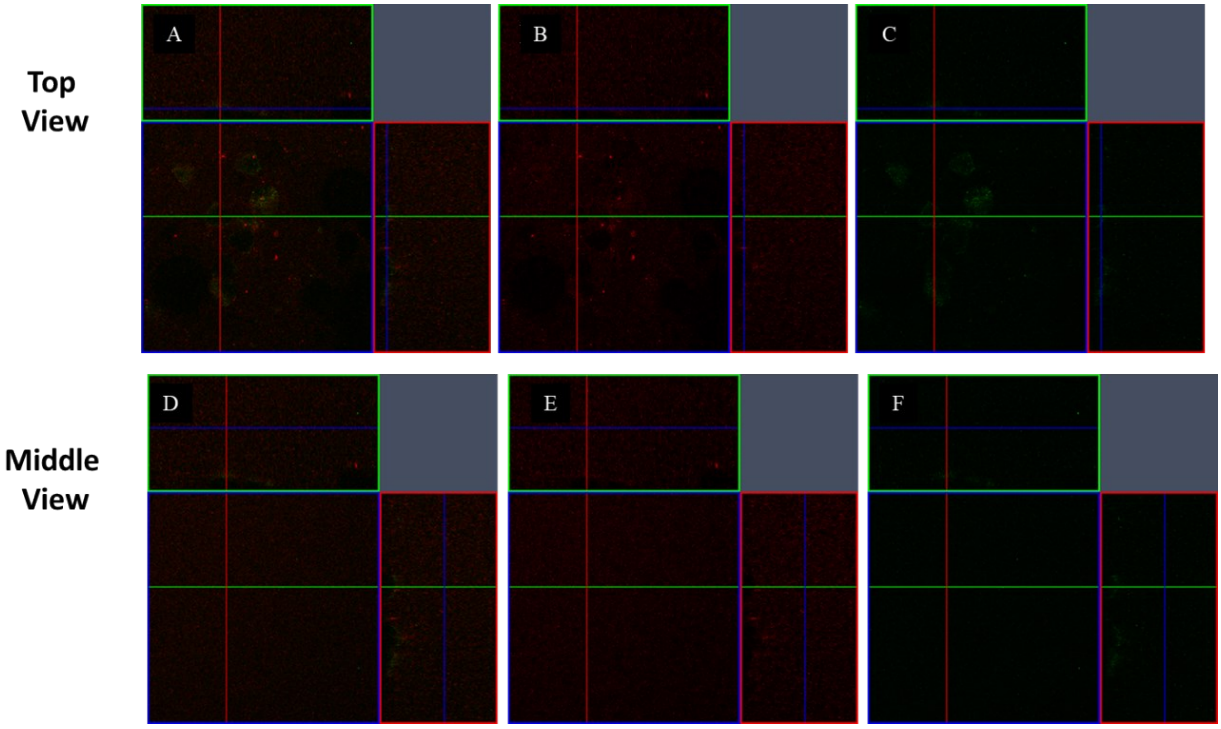


**Figure S6:** Release test of 600 µm microneedles loaded with the Standard MPs in the in vitro skin equivalent model after 2h; top and middle view. A-D) Merge of green and red channels; B-E) red channel; C-F) green channel.

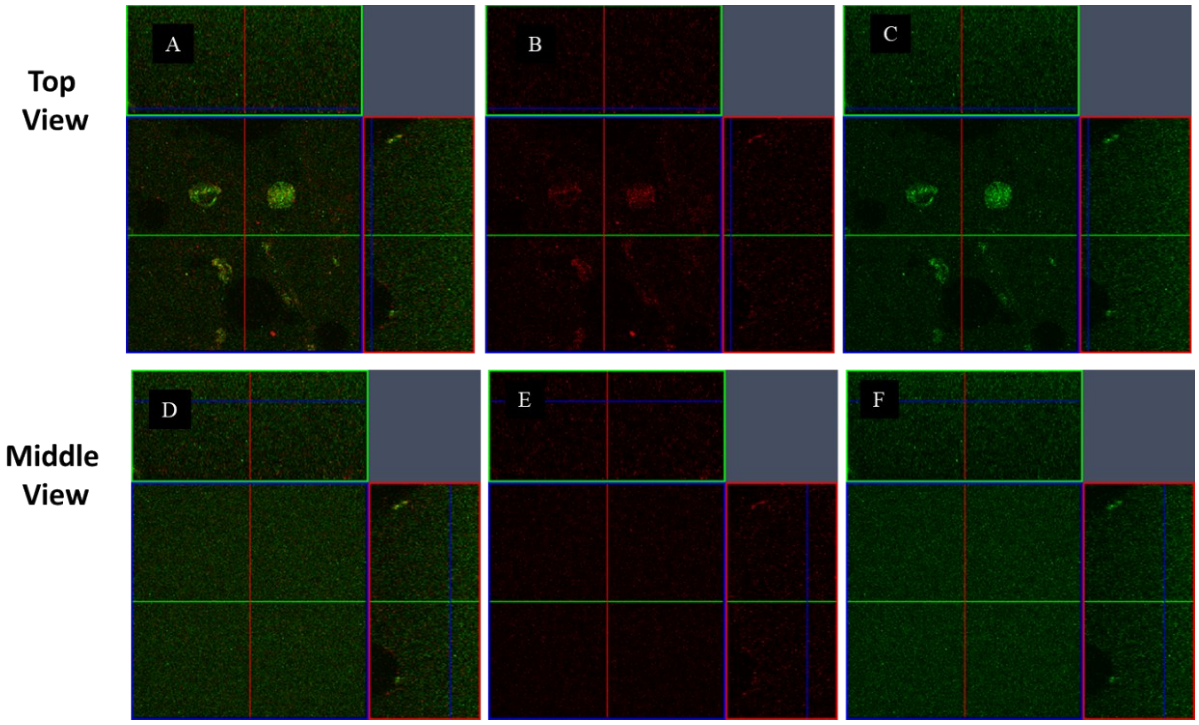


**Figure S7:** Release test of 600 µm microneedles loaded with the Standard MPs in the in vitro skin equivalent model after 24h; top and middle view. A-D) Merge of green and red channels; B-E) red channel; C-F) green channel.

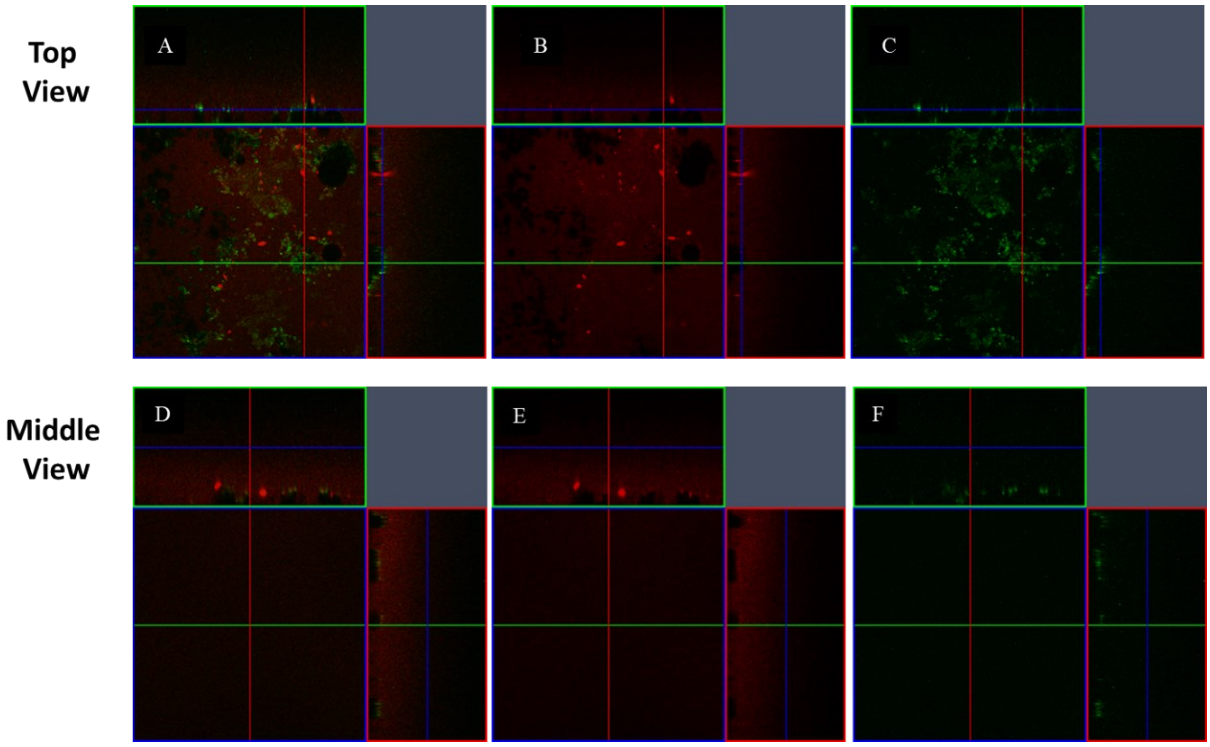


**Figure S8:** Release test of 600 µm microneedles loaded with the ABC- MPs in the in vitro skin equivalent model after 30 min; top and middle view. A) Merge of green and red channels; B) red channel; C) green channel.

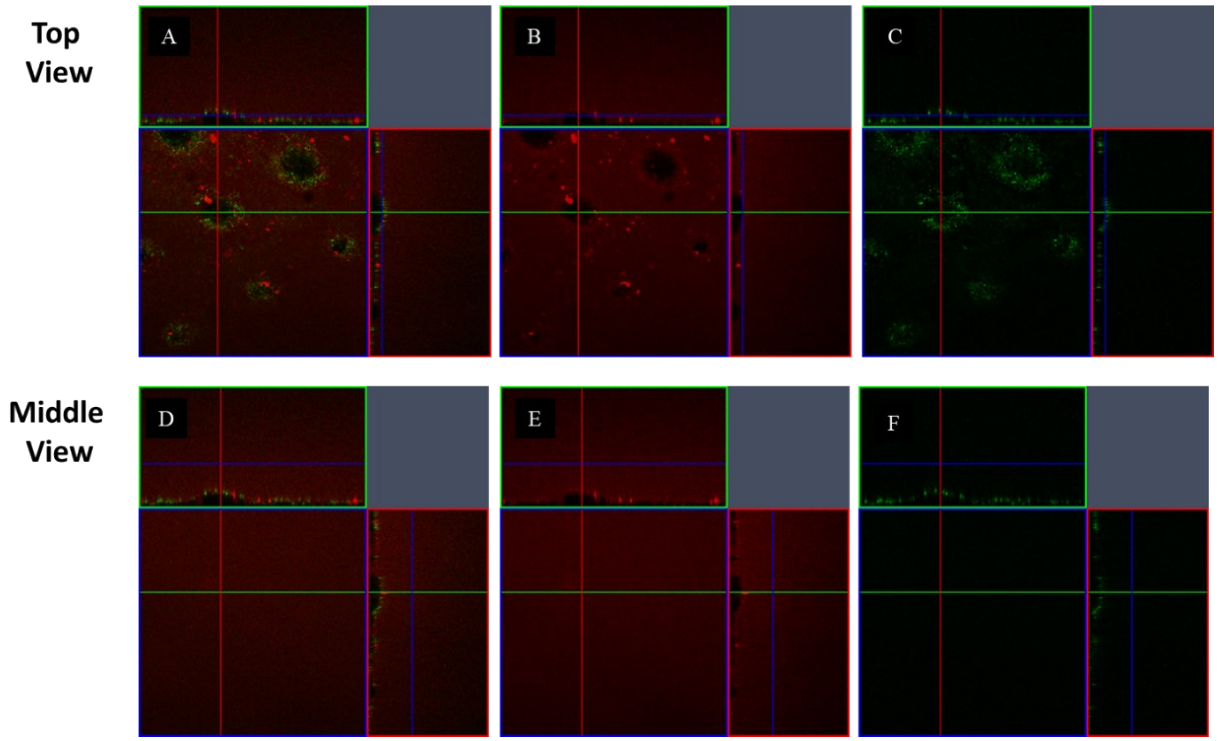


**Figure S9:** Release test of 600 µm microneedles loaded with the ABC- MPs in the in vitro skin equivalent model after 2h; top and middle view. A-D) Merge of green and red channels; B-E) red channel; C-F) green channel.

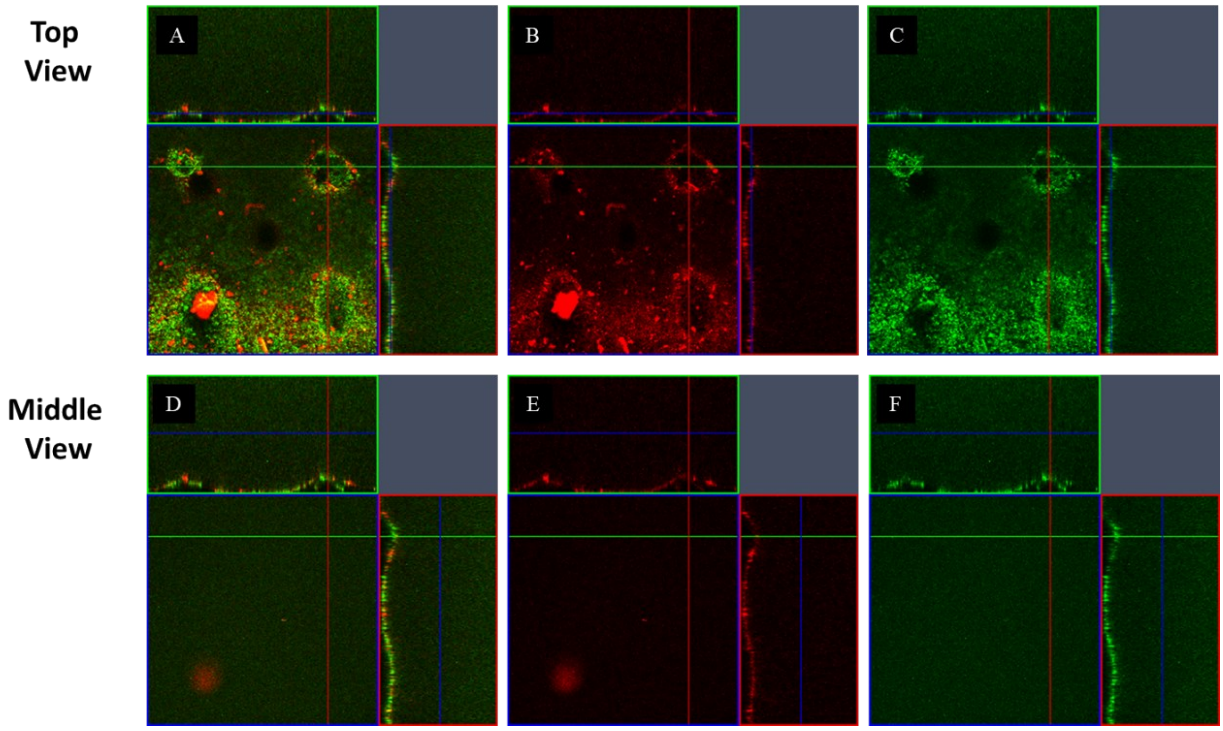


**Figure S10:** Release test of 600 µm microneedles loaded with the ABC- MPs in the in vitro skin equivalent model after 24h; top and middle view. A-D) Merge of green and red channels; B-E) red channel; C-F) green channel.

**Table S1.** Degree of loading (DOL) and % of activity of Collagenase after ATTO-488 and ATTO-740 conjugation.

| Collagenase | DOL | % Activity |
|---|---|---|
| ATTO-488 | 2 | 70.26±0.2 |
| ATTO-740 | 1.67 | 9.17±2.1 |

**Table S2.** Collagenase ABC and standard MPs features.

| Collagenase -488 MPs | % η | % Release in 2h | $D_{average}$ (μm) |
|---|---|---|---|
| ABC | 93.43± 4.0 | 39.57±2.29 | 13.23±9.5 |
| Standard | 23.86± 2.3 | 8.45±1.08 | 9.62±4.61 |