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3 **Tailor-Making Fluorescent Hyaluronic Acid Microgels via Combining Microfluidics and**
4 **Photoclick Chemistry for Sustained and Localized Delivery of Herceptin in Tumor**
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24 **KEYWORDS:** *microgels, microfluidics, click reaction, protein release, cancer therapy*

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26 **ABSTRACT:** Antibody therapeutics though representing a most used biomedicine suffers
27 from poor *in vivo* stability, rapid degradation, and frequent injections. Here, we report that
28 fluorescent hyaluronic acid microgels (HMGs) tailor-made by combining microfluidics and
29 “tetrazole-alkene” photoclick chemistry enable sustained and localized delivery of Herceptin
30 in ovarian tumor. HMGs were obtained with defined size (25-50 μm), narrow size distribution,
31 high stability, and strong green fluorescence. Notably, HMGs exhibited a remarkably high
32 loading of proteins like Herceptin and IgG with a loading efficiency exceeding 90% at a
33 theoretical protein loading content of 30 wt.%. *In vitro* protein release experiments revealed a
34 sustained and hyaluronidase-dependent release of Herceptin from HMGs, in which 80.6% of
35 Herceptin was released at 1 U/mL hyaluronidase in 10 days. The released Herceptin
36 maintained its secondary structure and antitumor activity. *In vivo* imaging results
37 demonstrated obviously better tumoral retaining for Cy5-labeled Herceptin loaded HMGs
38 following subcutaneous injection than for free protein counterpart. Interestingly,
39 subcutaneous injection of Herceptin-loaded HMGs into SKOV-3 human ovarian
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