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## Cell-borne 2D nanomaterials for efficient cancer targeting and photothermal therapy

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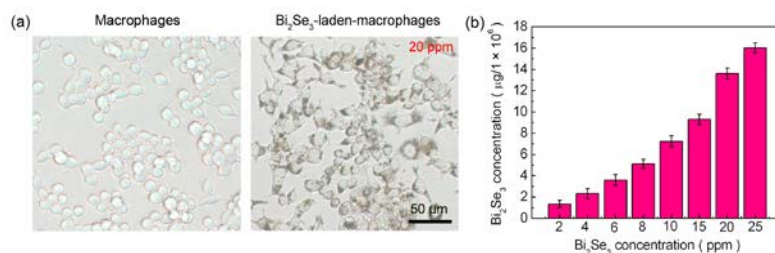
**Keywords:** 2D nanomaterials, Bi<sub>2</sub>Se<sub>3</sub> nanosheets, near-infrared, drug delivery, photothermal therapy

**Introduction:** Two of the challenges for clinical implementation of nano-therapeutic strategies are optimization of tumor targeting and clearance of the nanoagents *in vivo*. Herein, a cell-mediated therapy by transporting 2D Bi<sub>2</sub>Se<sub>3</sub> nanosheets within macrophage vehicles is described. The Bi<sub>2</sub>Se<sub>3</sub> nanosheets with excellent near-infrared photothermal performance exhibit high macrophage uptake and negligible cytotoxicity thus facilitating the fabrication of Bi<sub>2</sub>Se<sub>3</sub>-laden-macrophages. Compared with bare Bi<sub>2</sub>Se<sub>3</sub>, the Bi<sub>2</sub>Se<sub>3</sub>-laden-macrophages after intravenous injection show prolonged blood circulation and can overcome the hypoxia-associated drug delivery barrier to target the tumor efficiently and dramatically enhance the efficiency of photothermal cancer therapy. The Bi<sub>2</sub>Se<sub>3</sub>-laden-macrophages possess good biocompatibility as demonstrated by the biochemical and histological analyses and furthermore, most of the materials are excreted from the body within 25 days. Our findings reveal a desirable system for highly efficient near-infrared photothermal cancer therapy.

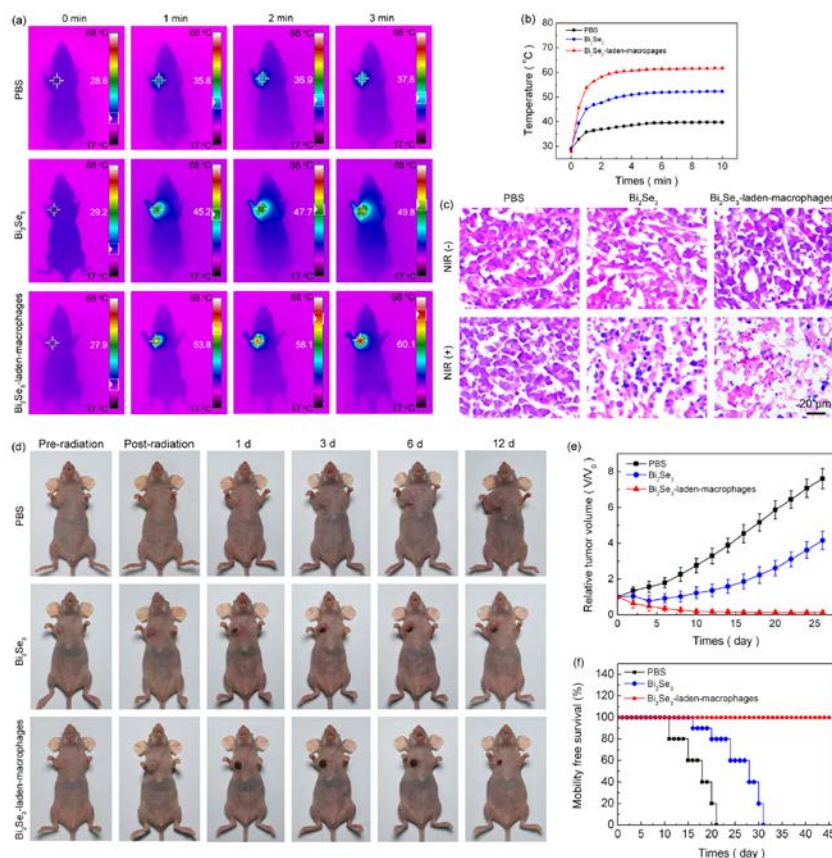
**Materials and Methods:** Bi<sub>2</sub>Se<sub>3</sub> nanosheets were prepared and characterized according to the method described previously [1]. The macrophages uptake of Bi<sub>2</sub>Se<sub>3</sub> nanosheets is analyzed by ICP-OES. The Bi<sub>2</sub>Se<sub>3</sub>-laden-macrophages *in vivo* photothermal cancer therapy were injected *via* the tail vein and irradiated (808 nm, 1.0 W/cm<sup>2</sup>) 10 min.

**Results and Discussion:** As shown in Fig. 1, the Bi<sub>2</sub>Se<sub>3</sub> nanosheets exhibit negligible cytotoxicity and high macrophage uptake efficiency. The good biocompatibility of Bi<sub>2</sub>Se<sub>3</sub> nanosheets is probably because Bi is an environmentally friendly element and Se is an essential trace element [2]. *In vivo* photothermal cancer therapy results demonstrate that Bi<sub>2</sub>Se<sub>3</sub>-laden-macrophages are efficient agents in photothermal ablation of tumors (Figure. 2).

**Conclusion:** Bi<sub>2</sub>Se<sub>3</sub>-laden-macrophages constitute an efficient delivery system in photothermal cancer therapy. The strategy utilizes macrophages as “Trojan horses” carrying 2D Bi<sub>2</sub>Se<sub>3</sub> nanosheets with high NIR photothermal performance, high macrophage uptake, and negligible cytotoxicity. The Bi<sub>2</sub>Se<sub>3</sub>-laden-macrophages constitute a highly efficient PTT system by optimizing the *in vivo* agent delivery and photothermal efficiency and this cell-mediated strategy can be further extended to other nanomaterials or drug-based therapies.



**Figure 1.** Macrophages uptake of  $\text{Bi}_2\text{Se}_3$  nanosheets: (a) Bright-field images of macrophages before and after uptake of  $\text{Bi}_2\text{Se}_3$  nanosheets; (b) Quantitative determination of macrophages uptake of  $\text{Bi}_2\text{Se}_3$  nanosheets.



**Figure 2.** *In vivo* photothermal cancer therapy of BALB/c nude mice bearing MCF-7 breast tumors under 10 min of NIR irradiation (808 nm,  $1.0 \text{ W/cm}^2$ ) at 24 h post-injection of PBS,  $\text{Bi}_2\text{Se}_3$  nanosheets, and  $\text{Bi}_2\text{Se}_3$ -laden-macrophages intravenously: (a) IR thermal images of the mice; (b) Curves of tumor temperature versus time; (c) H&E staining of tumor sections; (d) Typical mice before and after PTT treatments for 0, 1, 3, 6, and 12 days; (e) Tumor growth curves of different groups of mice; (f) Survival curves of different groups of mice.

### References:

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