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Ultrasensitive analysis of heat shock protein 90 $\alpha$  with antibodies orderly arrayed on a novel type of immunoprobe based on magnetic COFs

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## Abstract

The early diagnosis of liver cancer by target biomarkers is of great significance for improving the survival rate of cancer patients. However, it is still a challenging task to sensitively detect circulating protein biomarkers due to decreased binding activity of antibodies originating from uncontrolled orientation of immobilization on the surface of a solid matrix. In this work, a novel immunoaffinity probe, Fe<sub>3</sub>O<sub>4</sub>@TpBD-DSS-Ab-MEG, based on magnetic COFs with ordered arrangement of anchored antibodies has been developed and applied for the first time to detection of a cancer biomarker, heat shock protein 90 $\alpha$  (Hsp90 $\alpha$ ). The fabricated composites possess favorable features from magnetic cores and COF shells, including strong magnetic responses (7.96 emu g<sup>-1</sup>), ordered active groups, a large amount of immobilized antibodies (111.7  $\mu$ g/mg), good solvent and thermal stability. Fe<sub>3</sub>O<sub>4</sub>@TpBD-DSS-Ab-MEG demonstrated low detection limit (50 pg/mL), high selectivity (Hsp90 $\alpha$ :BSA=1:1000), desirable repeatability and good stability for

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