

# **Supporting Information**

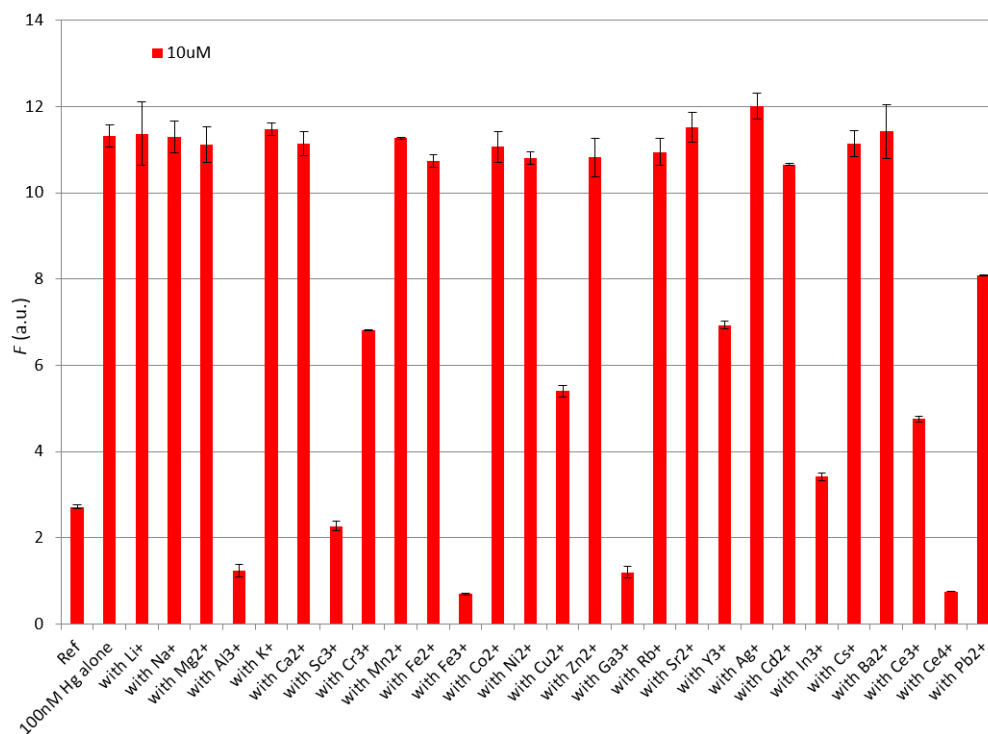
## **A Cleavable Molecular Beacon for Hg<sup>2+</sup> Detection based on Phosphorothioate RNA Modifications**

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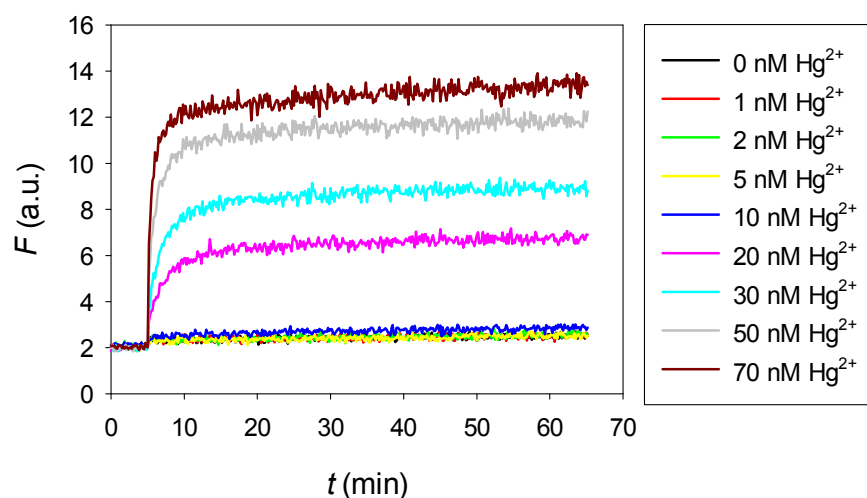
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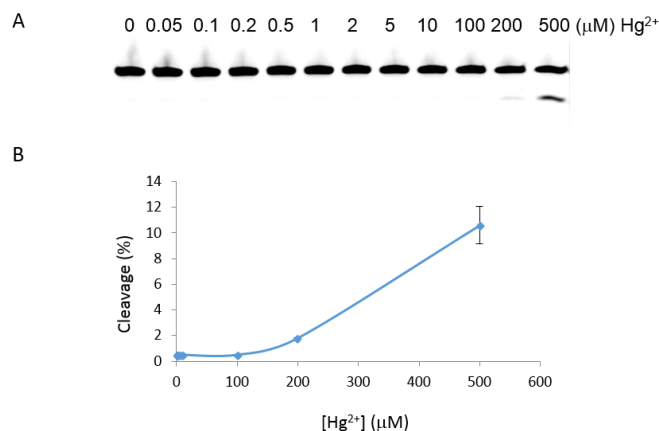
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**Figure S1.** Sensor response to 100 nM  $\text{Hg}^{2+}$  in the presence of 10  $\mu\text{M}$  of various metal ions. Among these, most monovalent and divalent metal ions do not interfere with  $\text{Hg}^{2+}$  sensing, but trivalent and tetravalent metal ions inhibited the signal, which is attributed to fluorescence quenching and DNA condensation by these high valent metal ions.



**Figure S2.** Sensor response in Lake Ontario water. The sample was prepared by mixing the Lake Ontario water with buffer at 1:1 ratio, and other operations were the same as that in buffer. We observed signal only with 20 nM  $\text{Hg}^{2+}$  or higher, suggesting that certain chemicals in the lake water can tightly bind  $\text{Hg}^{2+}$ . Once that binding is saturated,  $\text{Hg}^{2+}$  can still be sensitively detected.



**Figure S3.** (A) Gel-based cleavage assay of the PS-substrate in homogenized fish tissue. Unlike the reaction in pure buffer, the cleavage pattern in homogenized fish tissue is quite different. At low  $\text{Hg}^{2+}$  concentrations (e.g. below 100  $\mu\text{M}$ ), the cleavage is completely inhibited. Increased cleavage was observed only at higher concentrations. Note that the cleavage in clean buffers take place with nanomolar  $\text{Hg}^{2+}$ . Therefore, proteins and other molecules in the fish tissue can strongly sequester  $\text{Hg}^{2+}$  and even PS-modified RNA cannot compete efficiently with it. Since detecting such a high concentration of  $\text{Hg}^{2+}$  is unlikely to be physiologically useful, we do not pursue more biological samples. (B) Quantification of the results in (A). The fish tissue was prepared by weighing 600 mg of salmon meat (from a local supermarket). The meat was homogenized in 5 mL of buffer (25 mM NaCl, 50 mM MES pH 6) using Fisher Scientific PowerGen 125 omogenizer for 20 min. 5  $\mu\text{L}$  of the homogenized tissue was used for the assay in replacement of the normal buffer.