## **Supporting Information**

Ag Nanocube Coupled with Heating Enhanced DSN-Assisted Cycling Amplification for Surface-Enhanced Raman Spectroscopy Detection of microRNA-21

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## **Figure S1**

## Temperature characterization and calibration for the heated electrode

The surface of the heated electrode is indirectly heated by the internal heating-element that is controlled by the temperature-controller, resulting in a difference between the actual temperature of the electrode surface (T<sub>s</sub>) and the setting temperature of temperature-controller (T<sub>h</sub>), so the T<sub>s</sub> needs to be calibrated. We calibrate the relationship between T<sub>h</sub> and T<sub>s</sub> by the open circuit potential (OCP) method in 5 mM [Fe(CN)<sub>6</sub>]<sup>3-/4-</sup> + 0.5 M KCl solution. Put the heated electrode into the solution, then connect the heated electrode to the electrochemical workstation and temperature-controller. Change the T<sub>h</sub> in the temperature-controller at regular intervals, and record the corresponding potentials (Figure S1-A). Then the potentials can be converted to T<sub>s</sub> by the temperature-potential coefficient which is  $-1.56 \text{ mV}\cdot\text{K}^{-1}$  for 5 mM [Fe(CN)<sub>6</sub>]<sup>3-/4-</sup> + 0.5 M KCl solution. At last, we can obtain a linear

relationship between T<sub>s</sub> and T<sub>h</sub> (Figure S1-B). The linear regression equation was  $T_s = 0.944$  T<sub>h</sub> – 0.217 (R<sup>2</sup> = 0.9999). Later, once we set a T<sub>h</sub>, a corresponding T<sub>s</sub> can be obtained according to this linear equation. More details refer to ref <sup>39</sup>.

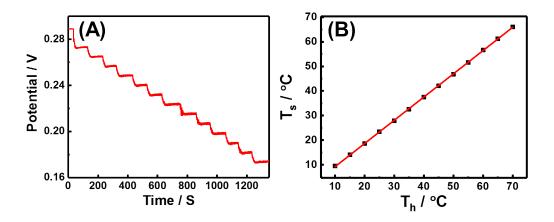


Figure S1. (A) The open circuit potential graph of heated electrode in 5 mM  $[Fe(CN)_6]^{3-/4-} + 0.5$  M KCl solution. (B) The linear relationship between surface temperature of the heated electrode  $(T_s)$  and the setting temperature of the temperature-controller  $(T_h)$ .

## Figure S2 Characterization of the stability of Au-S bonds

The dissociation of pDNA from the HAuE surface caused by the break of the Au-S bonds when the electrode is heated may cause false positive result. So we characterized the stability of Au-S bond by EIS at 55°C (the optimized electrode temperature). As can be seen in Figure S2,  $R_{ct}$  of pDNA/HAuE (Figure S2-a) was only slightly weakened after heated for 60 min at 55°C (Figure S2b), suggesting the enough stability of Au-S bonds at 55°C in this work.

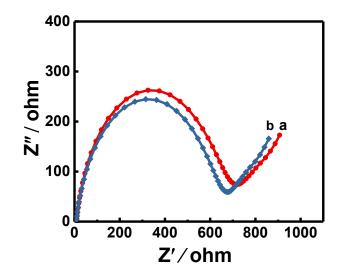


Figure S2. EIS curves of pDNA/HAuE before (a) and after (b) heated at 55°C for 60 min. The solution was 5 mM  $[Fe(CN)_6]^{3-/4-}$  containing 0.5 M KCl.