1 **Supporting Information**

2 A novel fluorescent digitonin derivative for non-invasive skin cholesterol detection:

3 Potential application in atherosclerosis screening

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5 *Jingshu Ni,[ab] Yong Liu,[abc] Haiou Hong,[d] Xiangyong Kong,[d] Yongsheng Han,[d] Lei Zhang,[e]*

6 *Yang Zhang,[ab] Yuanzhi Zhang,[ac] Changyi Hua,[a] Quanfu Wang,[a] Xia Wang,[a] Yao Huang,[ac]*

7 *Meili Dong[*ac] and YiKun Wang [*ac]*

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9 **Subjects' exclusion criteria**

10 Exclusion criteria included (a) current lipid-lowering therapy or lipid-lowering therapy within

11 the last year; (b) age under 18 years; (c) pregnancy; (d) psoriasis or dermatitis on one or the

12 other hand; (e) recent use (inside 24 h prior to testing) of skin drug, as a cream or moisturizer;

13 (f) chronic liver disease or evidence of abnormal liver function. (g) conditions that might lead

14 to an incomplete follow-up (i.e., life assumption a half year).

15 **Clinical information collection and grouping**

16 Age, sex, height, weight, smoking, history of diabetes, history of hypertension, medication

17 and other related information of subjects were collected. Antecubital venous blood were

18 collected for the measurement of total plasma cholesterol (TC), serum low-density lipoprotein

19 cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG),

20 glucose levels. The Framingham risk score is a simple and commonly used routine method for

21 evaluating coronary artery disease, and it is the most appropriate strategy for predicting the

22 individual's chance of developing cardiovascular disease (CVD) in long term. Since this risk

23 score gives a sign of the conceivable advantages of avoidance, it very well may be helpful for

24 both the patients and clinicians choosing whether way of life changes and preventive clinical

25 treatment. Absolute CVD risk percentage over 10 years was classified as low risk (< 10 %),

26 intermediate risk (10–20 %), and high risk (>20 %). Of the 266 subjects selected in Health

27 Management Center, 133 people had a score < 10% and 133 subjects with no conspicuous

28 stenosis of the vessel had a score ≥ 10 %. All 135 patients with overt vascular disease had a

29 score > 10 %, overt vascular disease was characterized as (a) stenosis of at least 50 % in at

30 least 1 vessel(any disease) and (b) stenosis of at least 50 % in ≥2 vessels (multivessel disease).

31 The principle motivation behind this clinical study is to investigate the distinction of skin

32 cholesterol content among low-risk group, risk group (intermediate risk and high risk) and

33 patients with cardiovascular disease. Along these lines, the participants were separated into

34 normal group, risk group and disease group, the normal group was with a FRS < 10%, the risk

35 group was with a FRS ≥ 10% and no vascular stenosis, and the disease group was with a

36 FRS≥ 10% and overt vascular disease.

37 **The hardware architecture of the detection system**

38 The optical system, as depicted in Figure S 3 , consists of a LED light source with a central

39 wavelength of 405 nm (LED405E, THORLABS), filter (diameter:12 mm, Central wavelength:

40 405 nm, bandwidth: 12 nm , HB-OPTICAL), couple lens assembly(diameter:12 mm, Giai

41 photnics Co.,ltd), a photodiode(SM05PD1A, THORLABS), a spectrometer(FX2000-RD,

42 346-1134 nm, 100 um slit, Fuxiang Optics) and an computer. The LED source with a central

43 wavelength of 405 nm was chosen as the light source because the excitation efficiency is

44 highest at 405 nm according to three-dimensional fluorescence spectrum of the FDD. The

45 light from the LED is coupled into the quartz fiber bundle through the filter and coupling lens,

46 which is divided into two ways, one way serves as the reference light signal to reach the

47 photodiode through the fiber, the other way serves as excitation light transmitted to the optical

48 fiber probe. The emission fluorescence is collected by the optical fiber probe and transmitted

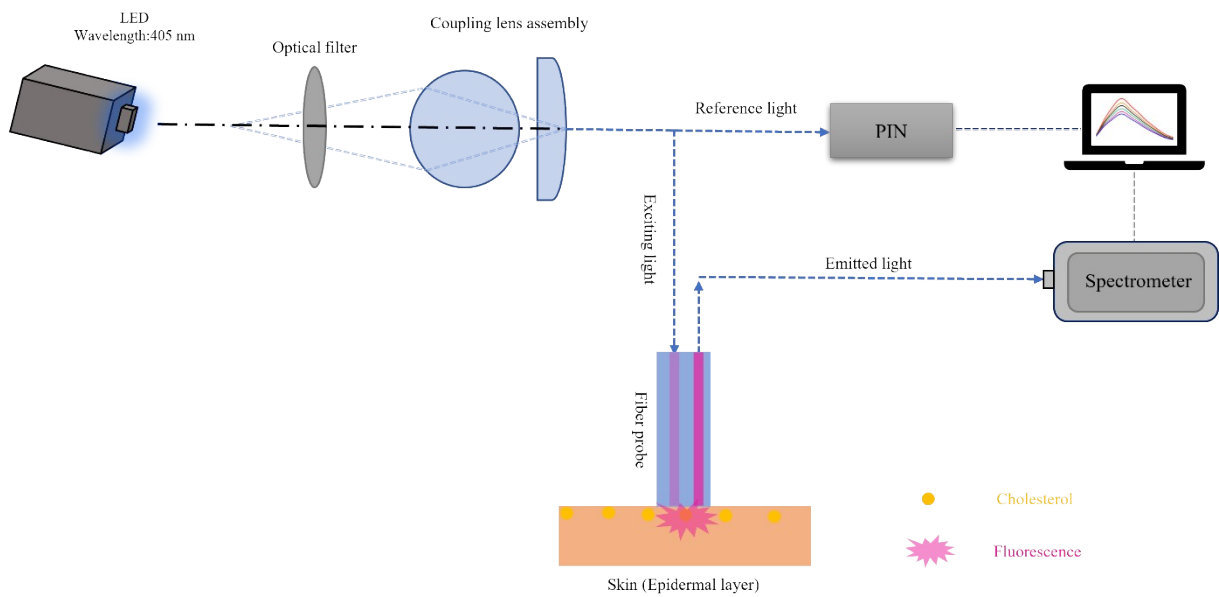49 to the spectrometer, the spectrum of the sample to be tested can be obtained.
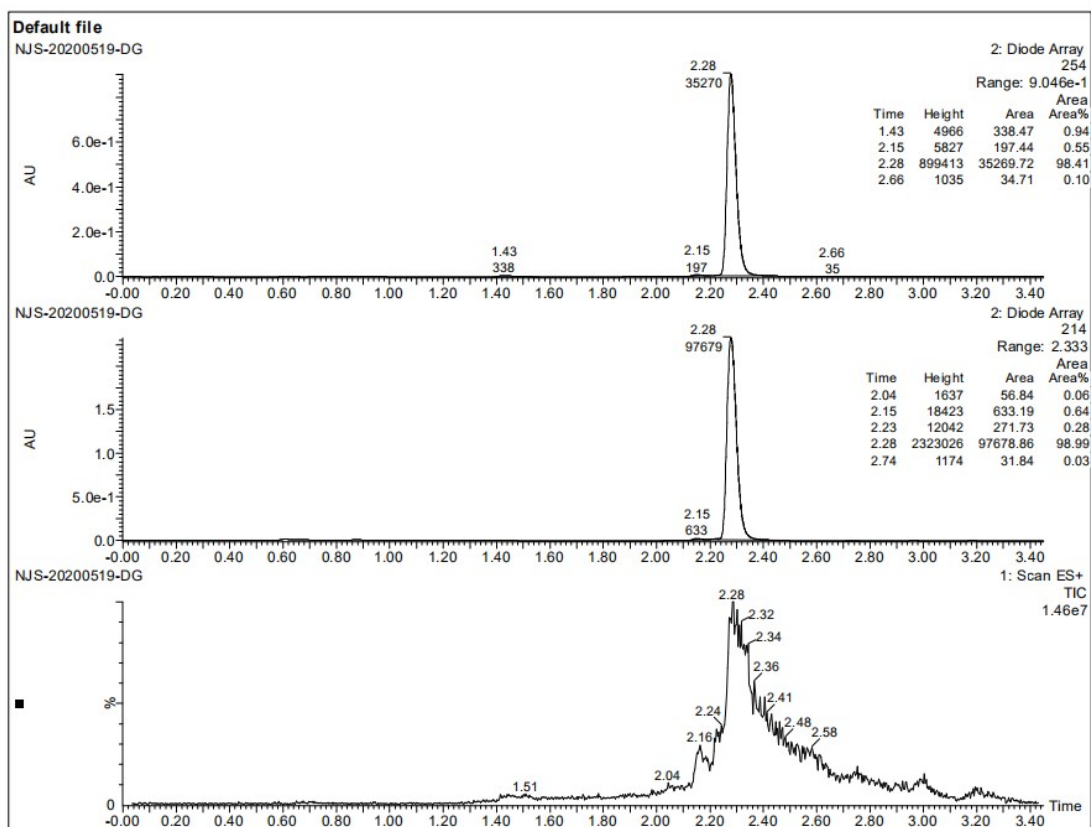
51 **Figure S1.** Purity of FDD separated by preparative liquid phase

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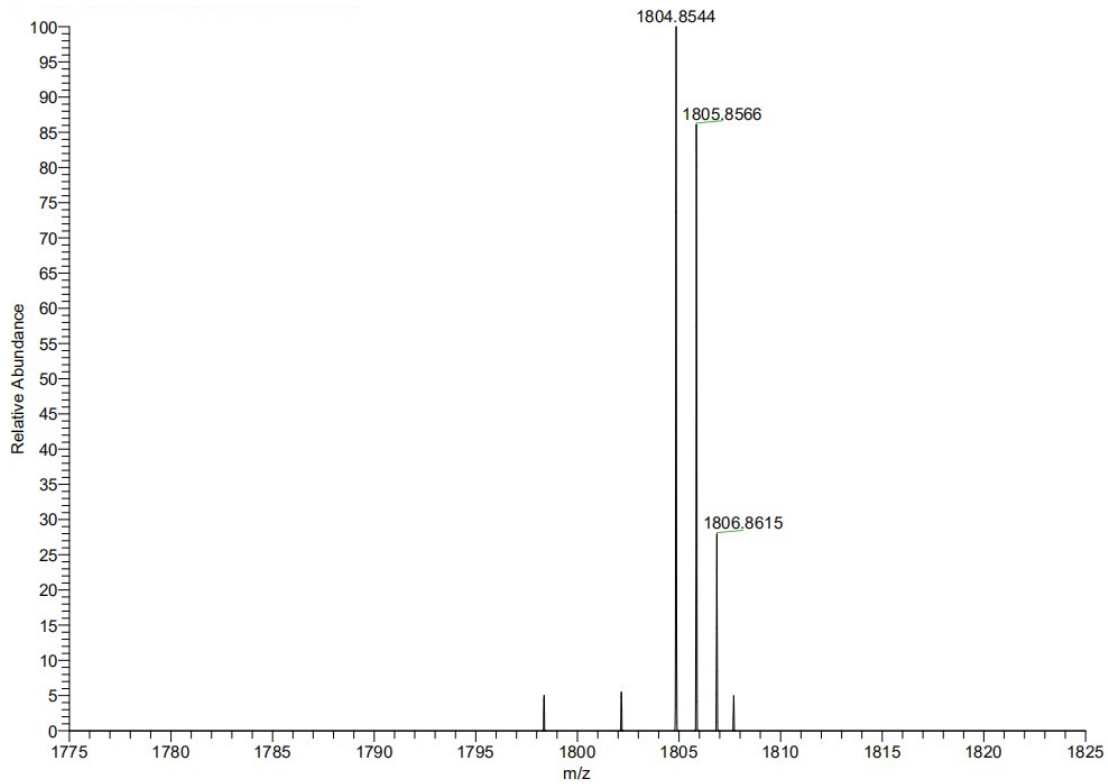
Figure S2. High resolution mass spectrometry of purified FDD

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Figure S3. Schematic of optical system for non-invasive detection of skin cholesterol

Table S1. Physiologic correlation of skin cholesterol measurement as assessed by univariate

analysis

	Correlation coefficient	P value
BMI	0.45	0.26

Blood glucose	0.41	0.32
Systolic blood pressure	0.39	0.19
TC (mmol/L)	0.51	0.05
LDL-C (mmol/L)	0.49	0.04
HDL-C (mmol/L)	0.55	0.08
TG	0.46	0.21

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