Supplement *(Measurement of serum protein markers)*

Thirteen biomarkers were measured and screened for this study as follows;

HE4 and LRG-1 were measured by enzyme-linked immunosorbent assay (ELISA). Briefly, 1μg/ml of capture antibodies to human HE4 (XEMA Co. Ltd., Moscow, Russia) or LRG1 (R&D systems, Minneapolis, MN) were added to a 96-well plate (Nalgene Nunc Inc., Rochester NY) and incubated overnight at 4°C. After blocking with phosphate buffered saline (PBS) containing 5% skim milk for 2 hours at room temperature, 100μl of serum samples or calibrators were added to a 96-well plate and incubated at room temperature for 1 hour. After washing three times with PBS containing 0.05% Tween 20, biotinylated detection antibodies to HE4 (XEMA) or LRG1 (R&D systems) were added and reactions were allowed to proceed for 1 hour at room temperature. After washing, 0.5μg/ml streptavidin–horseradish–peroxidase (Sigma-Aldrich, St. Louis, MO) was added, and the reaction was again allowed to proceed for 30 min at room temperature. After washing, 100 μl of tetramethylbenzidine substrate solution (KPL, Gaithersburg, MD) was added to induce a color reaction for 15 min, and 50 μl of 2N H2SO4 was used to stop the reaction. A microplate reader (Emax; Molecular Devices LLC., Sunnyvale, CA) was used to measure the optical density (OD) at 450 nm. The standard curves were established with OD450 as Y axis and the concentration of standard substance as X axis. Protein concentrations were calculated using a 5-parametric curve fit as part of the Softmax software (Molecular Devices). Calibration standard was purchased from XEMA (HE4) or R&D systems (LRG1).

Multiplexed serum Immunoassay of RANTES and sVCAM-1 were performed using the xMAP technology platform (Luminex Corp. Austin, TX) and carbodiimide coupling of capture antibodies to the MagPlex microspheres (Luminex Corp.) was done by the protocol.
recommended by the manufacturer. Microspheres were protected from prolonged exposure to light throughout these procedures. Briefly, the stock uncoupled MagPlex beads were resuspended by vortexing and sonication for approximately 20 seconds and then 1x10^6 beads were transferred to a microcentrifuge tube, washed with 100 μl of deionized water, and resuspended in 80 μl 0.1 M sodium phosphate (monobasic), pH 6.2. To activate the beads 10 μl of 50 mg/mL sulfo-NHS (N-hydroxysulfosuccinimide; ThermoFisher Scientific, Waltham, MA) and 10 μl of 50 mg/mL EDC (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride; ThermoFisher Scientific) were added to the beads and mixed gently by vortex. The bead suspension was incubated for 20 min at room temperature with gentle mixing by vortex at 10 minute intervals. Then the activated beads were washed twice with 250 μl of 0.05 M MES, pH 5.0 by vortex and sonication for approximately 20 seconds and resuspended in 100 μl of the same buffer. 10 μg of anti-RANTES (R&D systems) or anti-sVCAM-1 antibody (R&D systems) was added to the mixture and the reaction was incubated for 2 hours at room temperature with mixing by rotation. The microspheres were then washed twice with PBS-TBN buffer (0.02% Tween-20, 1% of BSA, and 0.05% sodium azide in PBS, pH 7.4), counted using hemocytometer, and stored at 2-8°C in the dark. Mixtures of two antibody-conjugated microspheres and 20 ul of serum samples or calibrators were added to a 96-well plate and incubated at room temperature for 1 hour. After then 20 ul of biotinylated detection antibodies to RANTES (R&D systems) and sVCAM-1 (R&D systems) were added and reactions were allowed to proceed for 1 hour at room temperature. Finally, the complex was incubated with 20 ul of streptavidin-phycoerythrin (Jackson ImmunoResearch Inc., West Grove, PA) for 30 minutes in the dark with agitation. The resulting bead complex was washed 2 times with PBS containing 0.05% Tween 20, resuspended in the same buffer, and analyzed with the Luminex 200 system. The standard curves were established with MFI (median fluorescence intensity) as Y axis and the concentration of calibrators as X axis.
Protein concentrations were calculated using a 5-parametric curve fit as part of the Bead View software (Upstate Biotechnology Inc., Lake Placid, NY). Calibration standards were purchased from PeproTech (RANTES; Rocky Hill, NJ) or R&D systems (sVCAM-1)

ApoA1, ApoA2, and B2M were measured on the Clinical Analyzer 7080(Hitachi Medical Corp., Japan) by immunoturbidimetric method; CA125, CA19.9, CEA, and CYFRA21.1 were measured on the Cobas e601(Hoffmann-La Roche AG., Switzerland) using electrochemiluminescent detection; and CRP and TTR were measured on the BN2 System (Siemens AG., Germany) by means of immunonephelometry according to the manufacturer’s instructions.