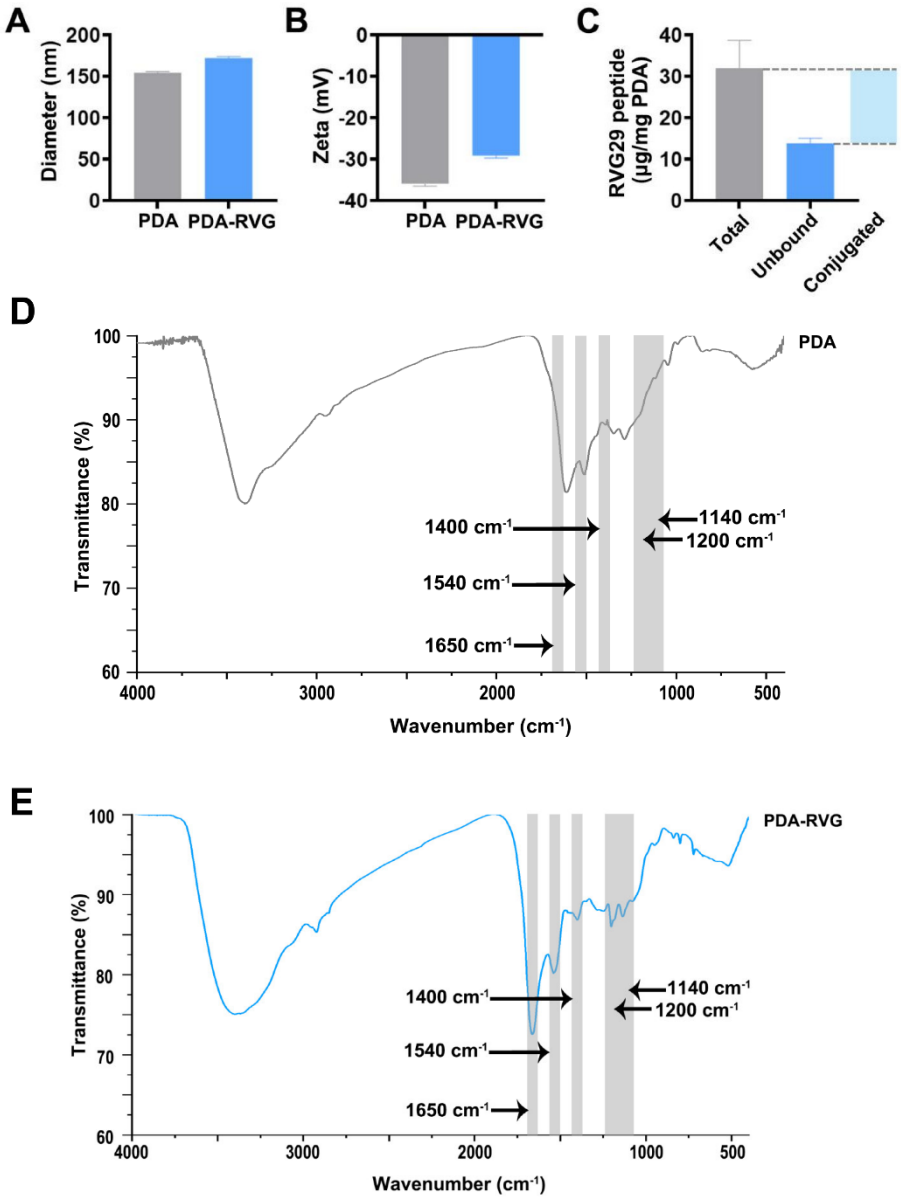

Figure S1. (A) PDA diameter and (B) zeta potential before and after RVG29 conjugated; n = 3. (C) Peptide Quantitation of RVG29; n = 3. (D, E) Representative FT-IR spectrum of PDA (D) and PDA-RVG (E).

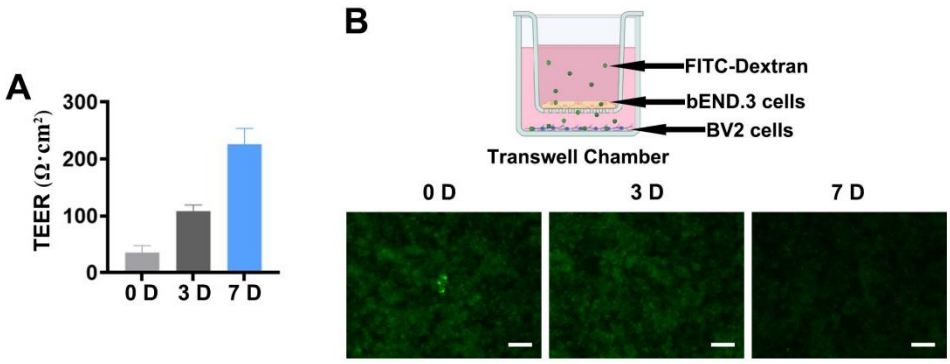

Figure S2. (A) Quantification analysis of values of TEER in different time of b.End.3 cells; n=8. (B) Schematic showing the *in vitro* model of the BBB with b.End.3 cells for permeability studies; Representative photomicrographs of FITC-dextran staining (Green) in different time of BV2 cells; scale bar = 30 μm.

Supplementary method 1

Characterization of PDA and PDA-RVG

The size distribution and zeta potential of PDA and PDA-RVG were measured using dynamic light scattering using a Zetasizer Nano ZS (Malvern Instruments Ltd., Worcestershire, UK). All measurements were performed in triplicate at room temperature. The conjugation of RVG29 polypeptide to PDA NPs were determined by Fourier transform infrared (FTIR) spectroscopy analysis. Briefly, PDA-RVG was lyophilized, dispersed in KBr powder (1:100, w/w) and pressed into a thin pellet. The vibrational spectrum of each sample was measured at least six times (Nicole Summit X, Thermo Fisher, USA).

Peptide Quantitation of RVG29

The RVG29 polypeptide was conjugated onto PDA NPs using the aforementioned method, and the resulting PDA-RVG conjugates were isolated by centrifugation at 15,000 rpm for 15 minutes. The amount of RVG29 conjugated onto the PDA NPs was accurately determined by measuring both the total initial RVG29 peptide concentration and the concentration of unbound peptide in the supernatant after centrifugation using a fluorescence amine assay.

Transendothelial electrical resistance (TEER) measurement

TEER was measured periodically to monitor the development of tight junctions. bEnd.3 cells ($2x10^5$/well) were seeded on the apical side of the transwell (2.0 μm pore size, Millipore) in a 12-well tissue culture plate. Fresh medium (0.5 mL within the insert and 1.5 mL in the outer well) was provided every other day. TEER was measured using a Millicell Electrical Resistance System (Millicell-ERS-2, Millipore). The short electrode was placed into the culture medium on the apical side of the transwell with no contact with bEnd.3 cells. The long electrode was placed into the medium of the lower chamber of the transwell. The TEER peak was used as an evaluation criterion for the formation of bEnd.3 cells tight junctions. The results were expressed as $\Omega \cdot cm^2$ of the cell surface.

BBB permeability assays

To determine BBB permeability, we used non-contact bEnd.3-BV2 co-culture model to represent the BBB *in vitro*. BV2 cells ($5x10^5$/well) were seeded at the bottom of the lower compartment of the transwell in 12-well tissue culture plates. We transferred the chambers with three different times of bEnd.3 cells to 12-well plates seeded with BV2 cells. After incubating at 37℃ for 24 h, add 20 μl of 1 mg/ml FITC-dextran to the upper transwell chamber. After 4 h at 37℃, detect the fluorescence intensity in the BV2 cells using a fluorescence microscope (X810, Keyence, Japan).