

Figure S1. Indigo plant leaf extract was prepared using ethanol (tryptanthrin content, 3.6  $\mu\text{g/ml}$ ).

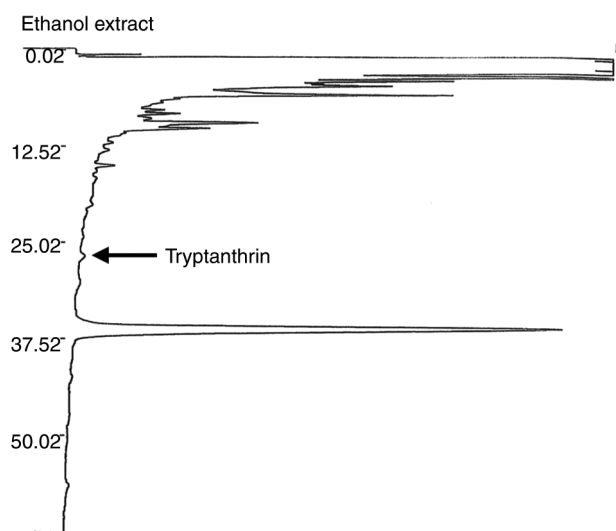


Figure S2. Differential interference contrast images of Fig. 3. ACE2, angiotensin-converting enzyme 2; dil, dilution; MDCK, Madin-Darby canine kidney. Scale bar, 50  $\mu$ m.

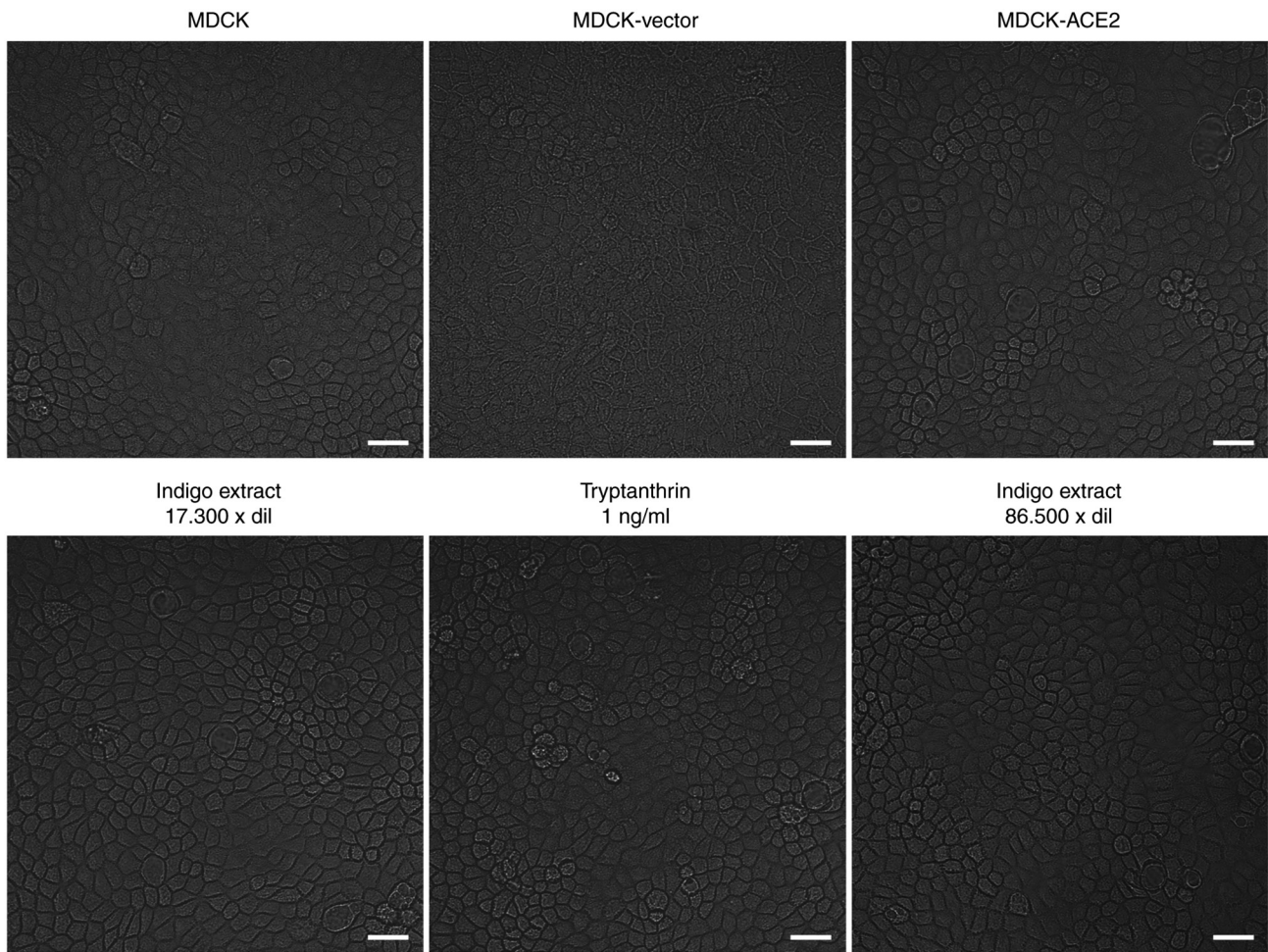


Figure S3. Mouse IgG labeled with fluorescein. MDCK-vector and MDCK-ACE2 cells were cultured overnight. Mouse IgG and S1 protein labeled with fluorescein (mIgG-fluorescein and S1-Fc-fluorescein, respectively) were added to the culture medium at a concentration of  $3 \mu\text{g/ml}$ , after which cells were observed alive through a confocal microscope. (A) A representative microphotograph is presented. Note that the fluorescent intensity of fluorescein (green) is comparable between the two wells containing mIgG-fluorescein or S1-Fc-fluorescein. After another day of incubation, cells were washed and the fluorescent intensities of fluorescein remaining on the cells were measured using a confocal laser microscopy system. (B) Representative photomicrographs with differential interference contrast images at the bottom. Below each image, the mean and standard deviation of the intensity (arbitrary unit) are presented for the corresponding experimental group.  $^aP < 2 \times 10^{-16}$  vs. MDCK-ACE2 cell intensity (scale bar,  $50 \mu\text{m}$ ). ACE2, angiotensin-converting enzyme 2; MDCK, Madin-Darby canine kidney.

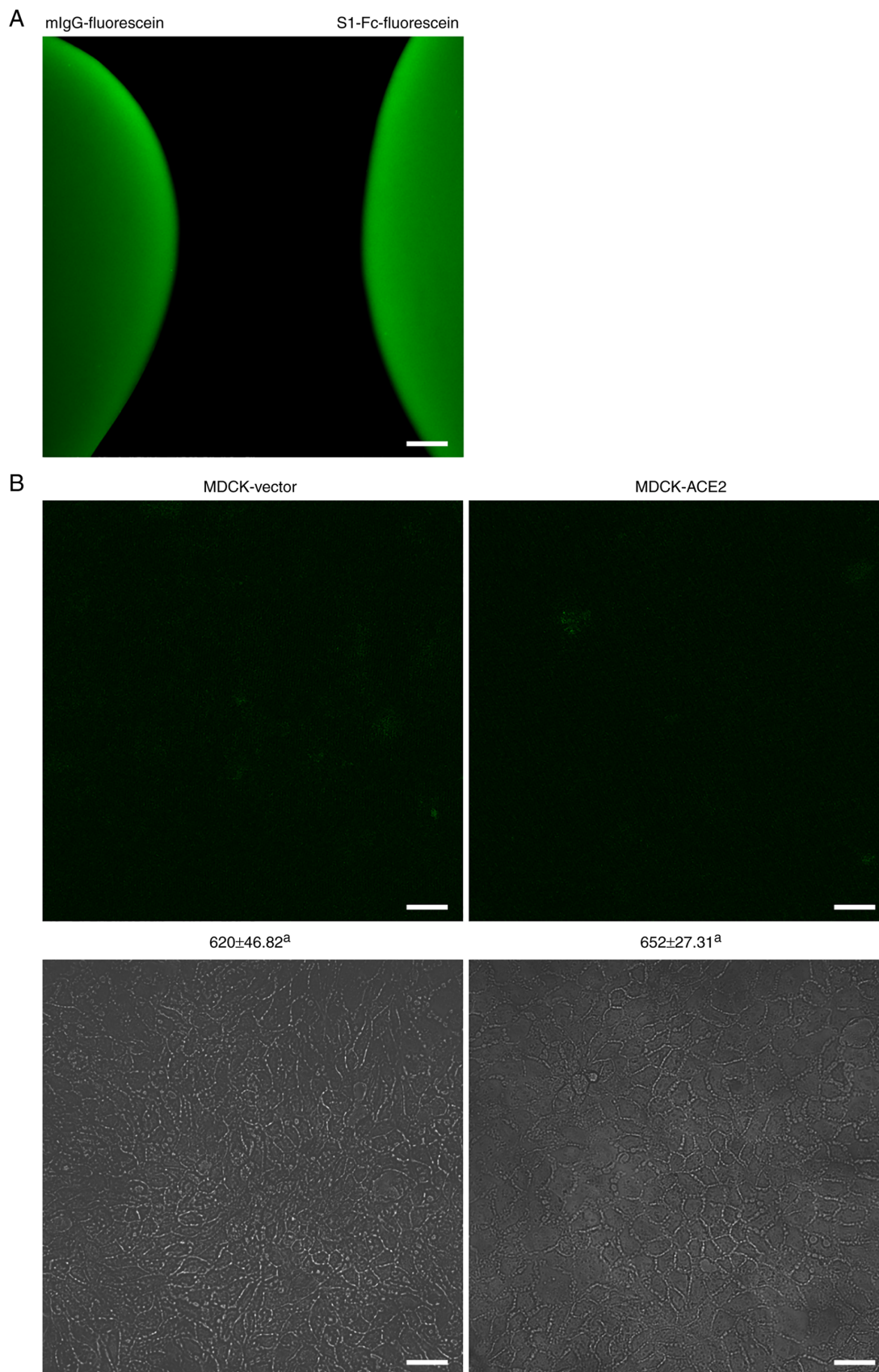


Table SI. P-value determination for fluorescence intensity of Fig. 3A, using one-way ANOVA and multiple comparison of Bonferroni correction.

Cell type or treatment group	MDCK	MDCK-vector	MDCK-ACE2	MDCK-ACE2	
				Indigo extract (17.300 x dil)	Indigo extract (86.500 x dil)
MDCK-vector	>0.999	-	-	-	-
MDCK-ACE2	<2x10 <sup>-16</sup>	<2x10 <sup>-16</sup>	-	-	-
Indigo extract 17.300 x dil	3.80x10 <sup>-8</sup>	1.60x10 <sup>-6</sup>	1.20x10 <sup>-13</sup>	-	-
Indigo extract 86.500 x dil	1.60x10 <sup>-13</sup>	2.30x10 <sup>-12</sup>	>0.999	9.20x10 <sup>-7</sup>	-
Tryptanthrin 1 ng/ml	6.10x10 <sup>-11</sup>	1.10x10 <sup>-9</sup>	0.0033	0.0027	0.8269

One-way ANOVA among all experimental groups: P=3.68x10<sup>-21</sup>. ACE2, angiotensin-converting enzyme 2; dil, dilution; MDCK, Madin-Darby canine kidney.