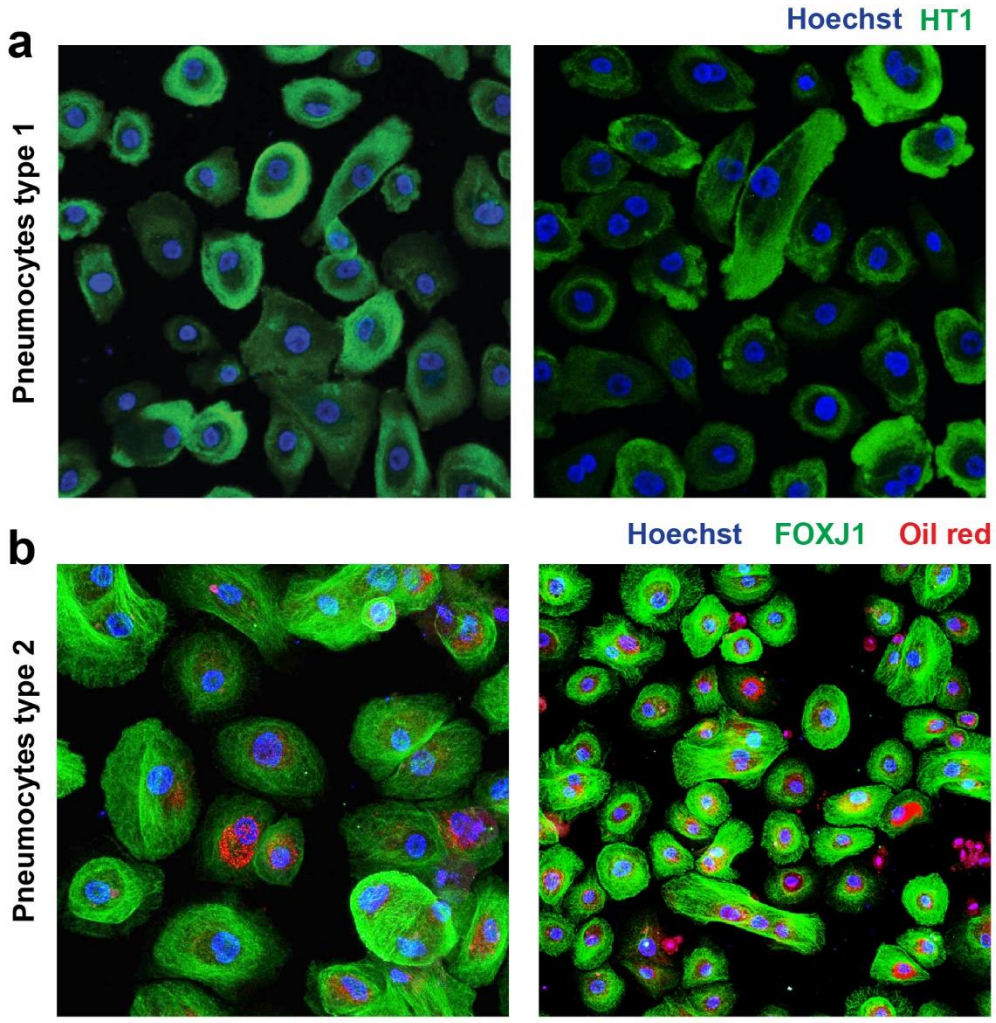
Elovanoids downregulate canonical SARS-CoV-2 cell-entry mediators and enhance protective signaling in human alveolar cells

Jorgelina Calandria[1], Surjyadipta Bhattacharjee[1], Marie-Audrey I. Kautzmann[1], Aram Asatryan[1], William C. Gordon[1], Khanh V. Do[1], Bokkyoo Jun[1], Pranab K. Mukherjee[1], Nicos A. Petasis[2], and Nicolas G. Bazan[1]*

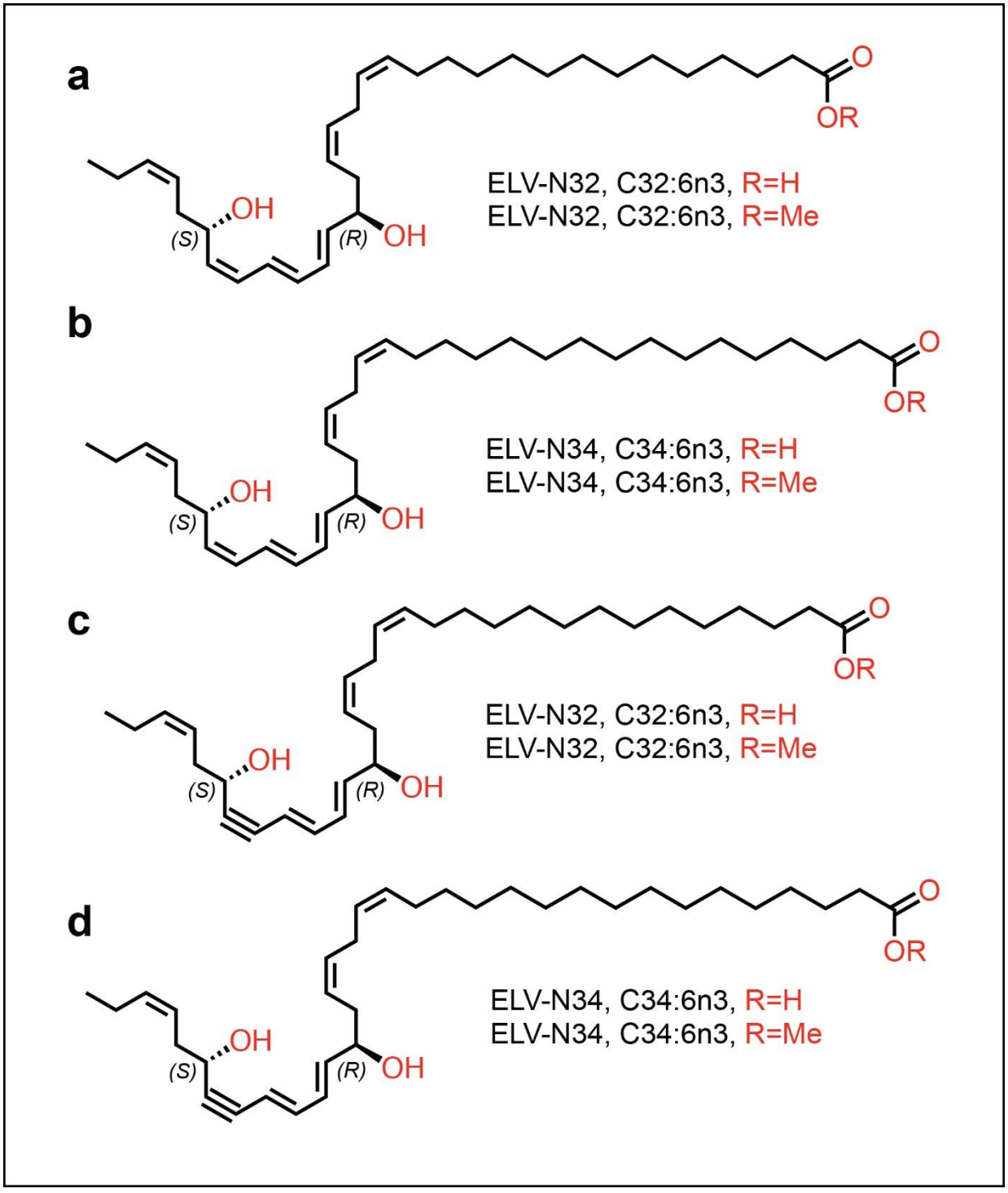
[1]Neuroscience Center of Excellence, School of Medicine, Louisiana State University Health New Orleans, 2020 Gravier Street, Suite D, New Orleans, USA.

[2]Department of Chemistry and Loker Hydrocarbon Research Institute, University of Southern California, Los Angeles, CA, USA.

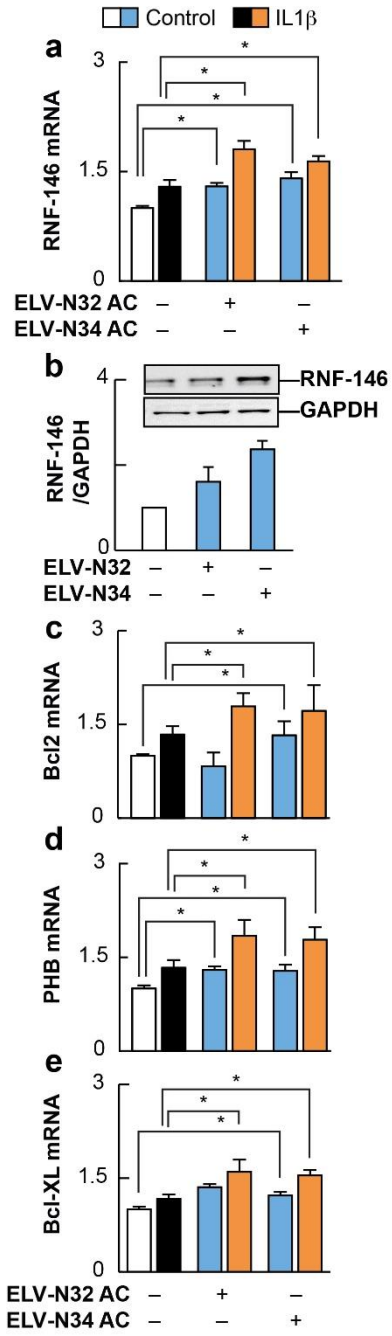
*Correspondence to: Nicolas G. Bazan, Neuroscience Center of Excellence, School of Medicine, Louisiana State University Health New Orleans, 2020 Gravier Street, Suite D, New Orleans, LA, 70112, USA; Phone: 504-599-0832; E-mail: nbazan@lsuhsc.edu.



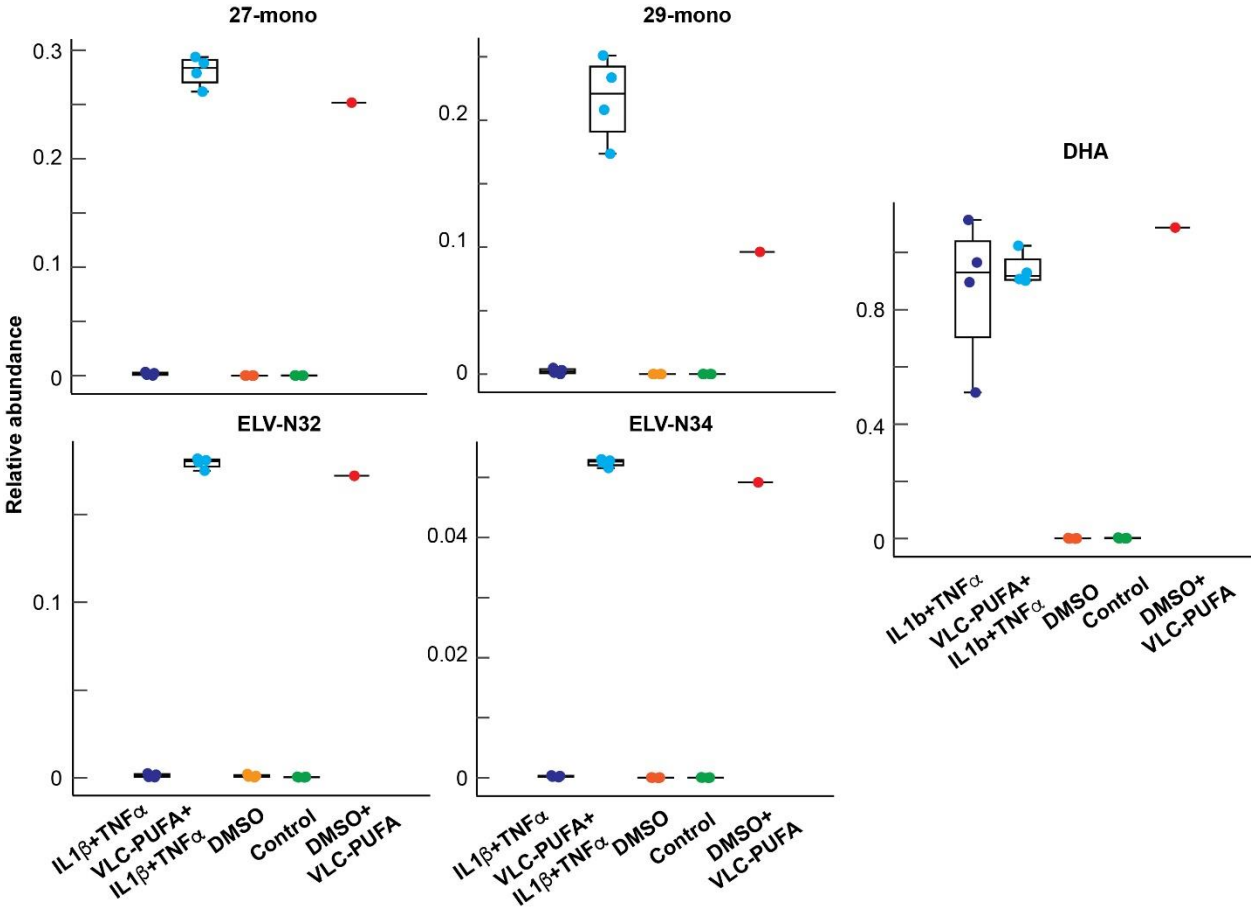
Extended Data Fig. 1. Pneumocyte markers in chamber slide cultures. Type I pneumocytes labeled (green) with the specific marker HT1-53 (upper panels). Type II lung pneumocytes labeled with a ciliated cell marker Foxj1 (green), which is required for cilia formation and is an early marker of epithelial cell differentiation, recovery, and function, and Oil Red O (red), a marker for the type II lipid/lamellar bodies (bottom panels). Nuclei were labeled with Hoechst (blue).



Extended Data Fig. 2. Chemical structures of the elovanoids N32 (top) and N34 (second). ELV-N32, R denotes the substituent in the carbon located is H = hydrogen or Me = methyl-ester. The third and fourth molecule from top to bottom shows the triple bond that make the molecules acetylenic.



Extended Data Fig. 3. a,c,d,e. Semi-quantitave real time PCR quantitation of target of elovanoids N32 and N34, RNF-146 (alias Iduna), Prohibitin (PHB), Bcl2 and Bcl-XL (Primers in Table 1), in alveolar cells exposed to the acetylene form of the ELVs for 24 hours in the presence or absence of 10ng/ml IL1β. **b,** Western blot assay on alveolar cells exposed for 24h to Elovanoids N32 and N34 with the substituent R=methyl ester.



Extended Data Fig. 4. Relative abundance of the elovanoids N32 and N34 (bottom panels) and their intermediates 27 mono-hydroxy and 29 mon-hydroxy (top panels) when the alveolar cells are exposed to the precursors VLC-PUFAs: 32:6 and 34:6 in the presence or absence of 10ng/ml IL1β and 10 ng/ml TNFα for 24 hours. DHA abundance was analyzed as a specificity control. The plot shows the box upper limit 3rd Quartile, bottom side 1st quartile, middle line: the median and the whiskers denote the maximum and minimum observations. *p<0.05 in t-test comparisons with the respective control. Repetition of the experiment of Fig. 2 in 24 well plates.