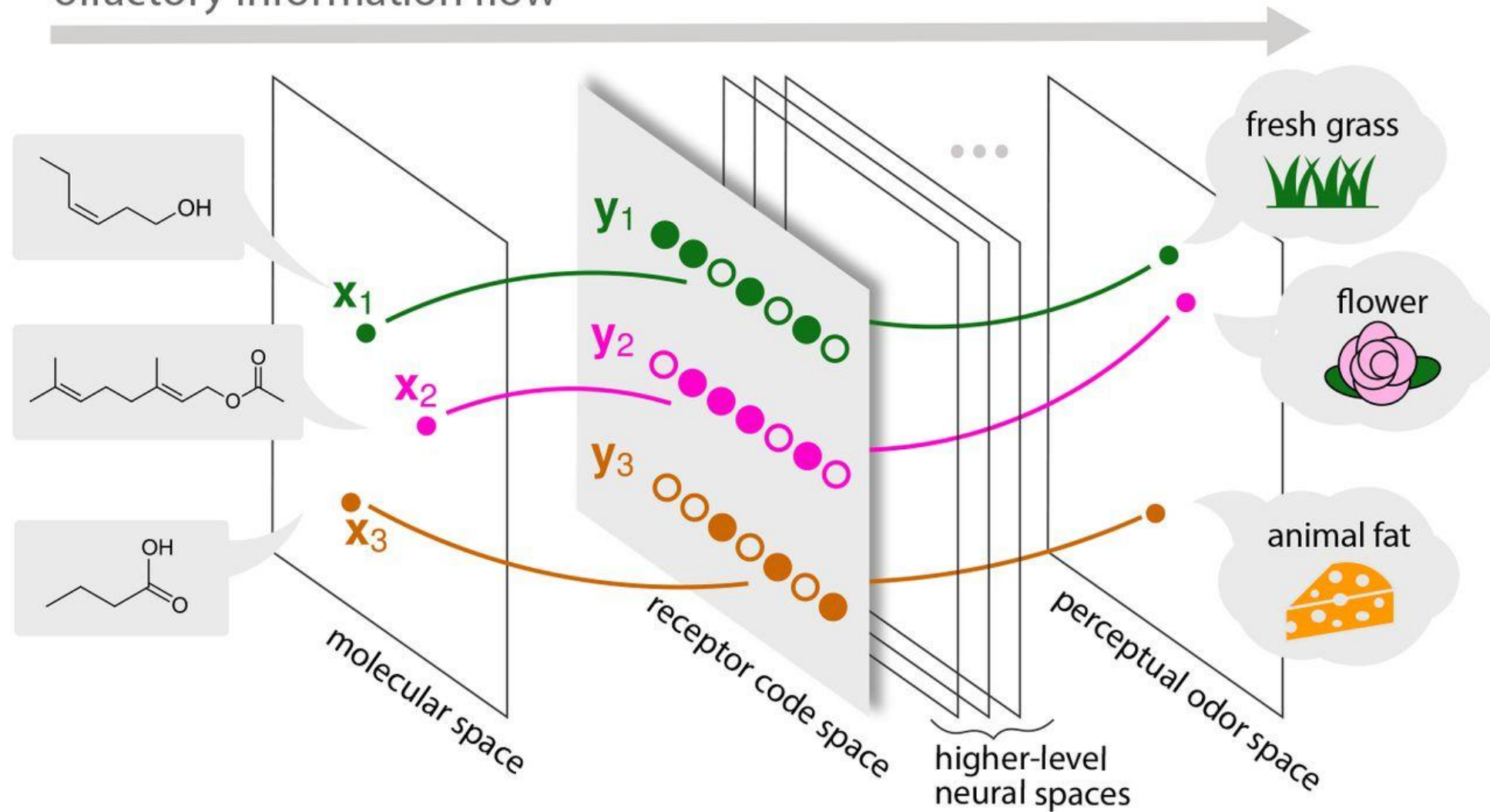














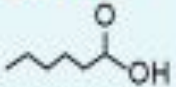

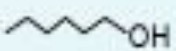


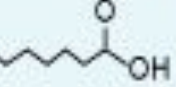










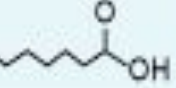








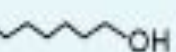




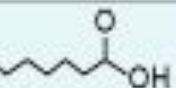
















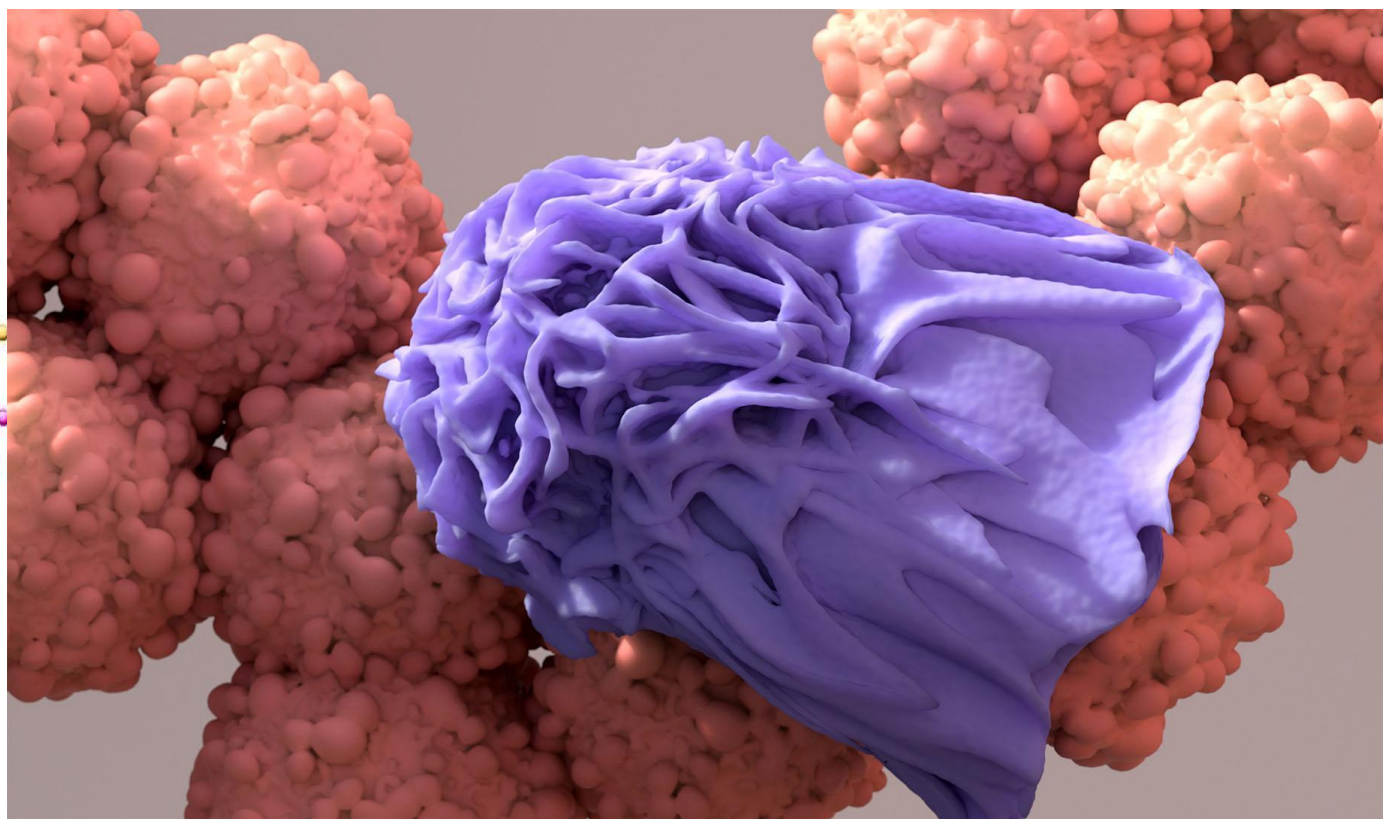
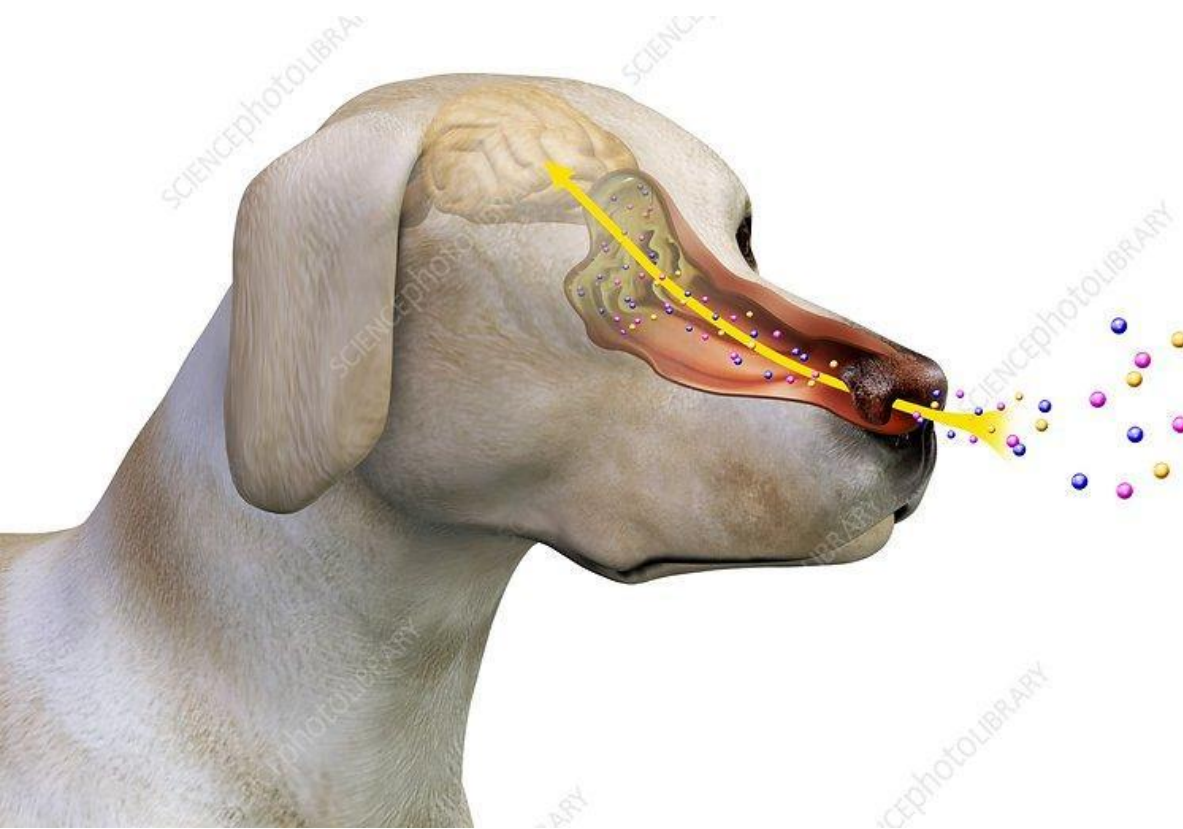
# olfactory information flow



**Modular structure of human olfactory receptor codes reflects the bases of odor perception**

Odorant receptors	 1	 2	 3	 4	 5	 6	 7	 8	 9	 10	 11	 12	 13	 14	
Odorants															Description
<b>A</b> 															rancid, sour, goat-like
<b>B</b> 															sweet, herbal, woody
<b>C</b> 															rancid, sour, sweaty
<b>D</b> 															violet, sweet, woody
<b>E</b> 															rancid, sour, repulsive
<b>F</b> 															sweet, orange, rose
<b>G</b> 															waxy, cheese, nut-like
<b>H</b> 															fresh, rose, oily floral

MODIFIED AFTER LINDA BUCK AND COLLEAGUES IN CELL VOL 96, MARCH 5, 1999





# Ectopically expressed olfactory receptors OR51E1 and OR51E2 suppress proliferation and promote cell death in a prostate cancer cell line

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Affiliations + expand

PMID: 33640452 PMCID: [PMC8024707](#) DOI: [10.1016/j.jbc.2021.100475](#)

## Abstract

Olfactory receptors (ORs), the largest family of G protein-coupled receptors, are expressed in the nasal epithelium where they mediate the sense of smell. However, ORs are also found in other non-nasal tissues, but the role of these ectopic ORs in cell signaling, proliferation, and survival is not well understood. Here, using an inducible expression system in the lymph node carcinoma of the prostate (LNCaP) cell line, we investigated two ectopic ORs, OR51E1 and OR51E2, which have been shown to be upregulated in prostate cancer. We found that, consistent with previous studies, OR51E1 stimulated adenylyl cyclase in response to treatment by short-chain to medium-chain organic acids (C3-C9) but not by acetate. OR51E2 responded to acetate and propionate but not to the longer chain organic acids. Stimulation of LNCaP cells with butyrate inhibited their growth, and the knockdown of the endogenous OR51E1 negated this cytostatic effect. Most significantly, overexpression of OR51E1 or OR51E2 suppressed LNCaP cell proliferation. Overexpression of another ectopic OR OR2AT4,  $\beta$ 2-adrenergic receptor, or treatment of cells with forskolin did not suppress cell proliferation, indicating that a rise in cAMP is not sufficient to induce cytostasis. Overexpression of OR51E1 caused an upregulation of cytostatic and cell death markers including p27, p21, and p53, strongly increased annexin V staining, and stimulated extracellular signal-regulated protein kinases 1 and 2. Overexpression and/or activation of OR51E1 did not affect human embryonic kidney 293 cell proliferation, indicating that cytotoxicity of OR51E1/OR51E2 is specific for LNCaP cells. Together, our results further our understanding of prostate cancer etiology and suggest that ectopic ORs may be useful therapeutic targets.

**Keywords:** G protein; G protein-coupled receptor; OR51E1; OR51E2; cAMP; cell death; olfactory; proliferation.

- In **hepatocarcinoma cells**, activation of **OR1A2** by citronellal leads to calcium signals and a reduction in cell proliferation
- In **non-small-cell lung cancer**, **OR2J3** expression increases upon helional application, and furthermore, the activation induces apoptosis and inhibits cell proliferation
- **OR51E2** shows a high, tumor-specific expression in **prostate cancer cells** in comparison to healthy prostate tissues ([13](#), [14](#)). Furthermore, activating the OR by its ligand  $\beta$ -ionone leads to the inhibition of cell proliferation

Weber L, Maßberg D, Becker C, Altmüller J, Ubrig B, Bonatz G, Wölk G, Philippou S, Tannapfel A, Hatt H and Gisselmann G (2018) Olfactory Receptors as Biomarkers in Human Breast Carcinoma Tissues. *Front. Oncol.* 8:33. doi: 10.3389/fonc.2018.00033

# Human ectopic olfactory receptors and their food originated ligands: a review

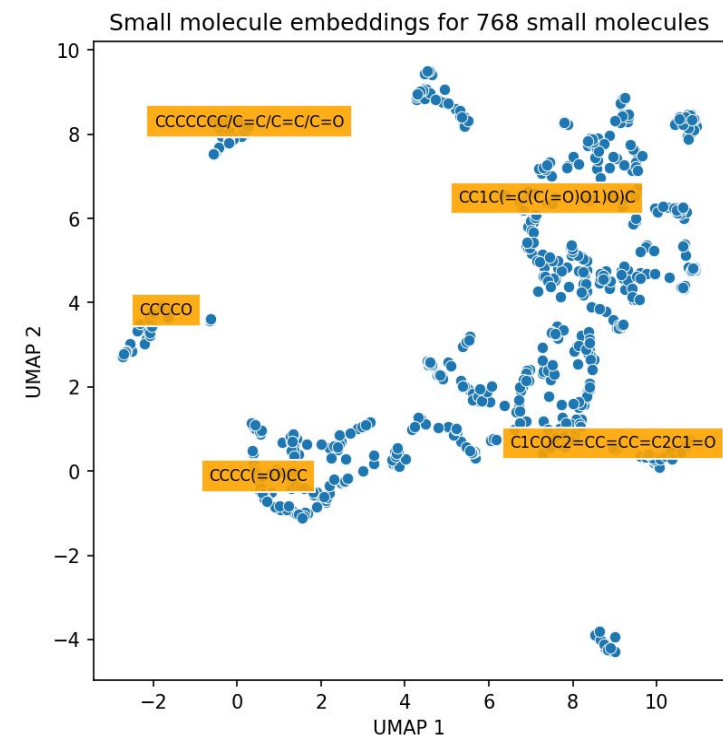
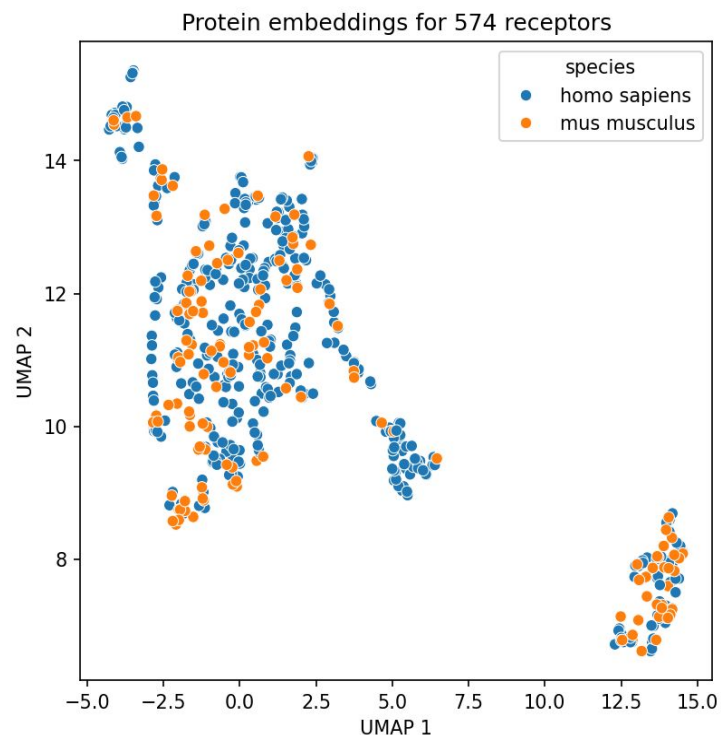
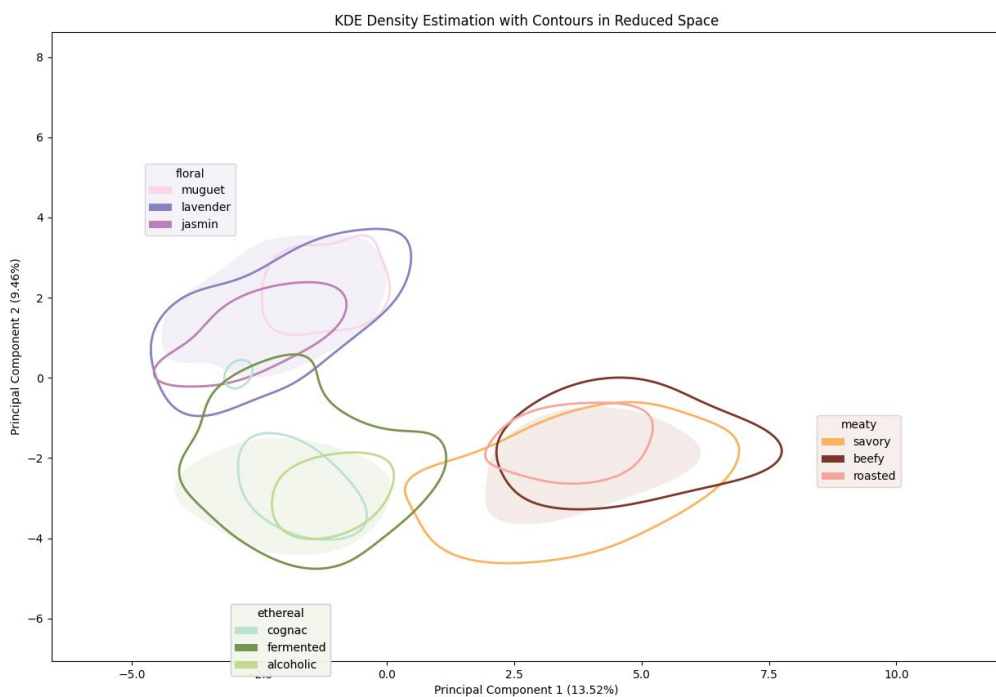
Rifat Nowshin Raka<sup>a,b,c,d,e</sup>, Hua Wu<sup>a,b,f</sup>, Junsong Xiao<sup>a,b,c,d,e</sup> , Imam Hossen<sup>a,b,c,d,e</sup>, Yanping Cao<sup>a,c</sup>, Mingquan Huang<sup>a,b</sup>, and Jianming Jin<sup>a,f</sup>

**Table 1.** EORs expressed in human body.

Tissue	Cell Source	EORs	Gene	Ligands	Detection Techniques	Ref.
Tongue	Taste cells from Human fungiform papilla cells (HBO cells)	OR2W1 OR5A1  OR5P3 OR51E1	<i>OR2W1/ hs6M1-15</i> <i>OR5A1/ OR5A1P/</i> <i>OST181/OR11-249</i> <i>OR5P3/ JCG1</i> <i>OR51E1/POGR/</i> <i>DGPCR/ PSGR2/</i> <i>DGPCR/GPR136/</i> <i>GPR164/</i> <i>OR51E1P/</i> <i>OR52A3P</i>	Heptanal, Eugenol, Acetophenone, Lylal, Coumarin, Hexanoic Acid	Immunocytochemistry, qRT-PCR, Single-cell calcium imaging, siRNA transfection	Malik et al. 2019
Fetal Tongue	Lingual epithelial cells from the tongue surface of a Caucasian adolescent patient	JCG6  TPCR85 JCG2 JCG9	<i>OR10A5/OR10A1/</i> <i>OR11-403</i> <i>OR8B8</i> <i>OR8D2</i> <i>OR8D1/ OR8D3/</i> <i>OST004/PDJ9J14</i>	–	RT-PCR	Durzyński et al. 2005
Adult tongue		HTPCR06   HGMP07I   JCG3 JCG5 OR4M1	<i>OR2K2/HSHTPCRH06/</i> <i>OR2AN1P/</i> <i>OR2AR1P/</i> <i>HTPCRH06</i> <i>OR1E1/OR1E5/</i> <i>OR1E6/OR17-2/</i> <i>OR1E8P/OR1E9P/</i> <i>OST547/OR13-66/</i> <i>OR17-32</i> <i>OR5P2/JCG4</i> <i>OR10A4/OR10A4P</i> <i>OR4M1/ OR14-7</i>	Acetophenone	cAMP assay, WB	Zhao et al. 2013
Brain	Traumatic Brain Injury Patient's brain					
Skin	Primary human keratinocyte	OR10G7	<i>OR10G7/OR11-283</i>	Acetophenone	RT-PCR, si-RNA, Transfection, Immunostaining	Tham et al. 2019
Blood	Peripheral blood mononuclear cells (PBMC)	OR11H1	<i>OR11H1/OR22-1/OR11H12</i>	–	Microarray, qRT-PCR	Zhao et al. 2013
Heart	Aorta, coronary artery, umbilical vein endothelial cells (HUVEC cell line)	OR10J5	<i>OR10J5/OR1-28</i>	Lylal	Matrigel plug assay, Calcium assay, siRNA, WB	Kim et al. 2015

# Data

- Protein receptor x Small molecule data from [M2OR](#) (~3k positives)
- Small molecule x Odor text labels from [Kaggle](#) (~500 positives)



# ML setup

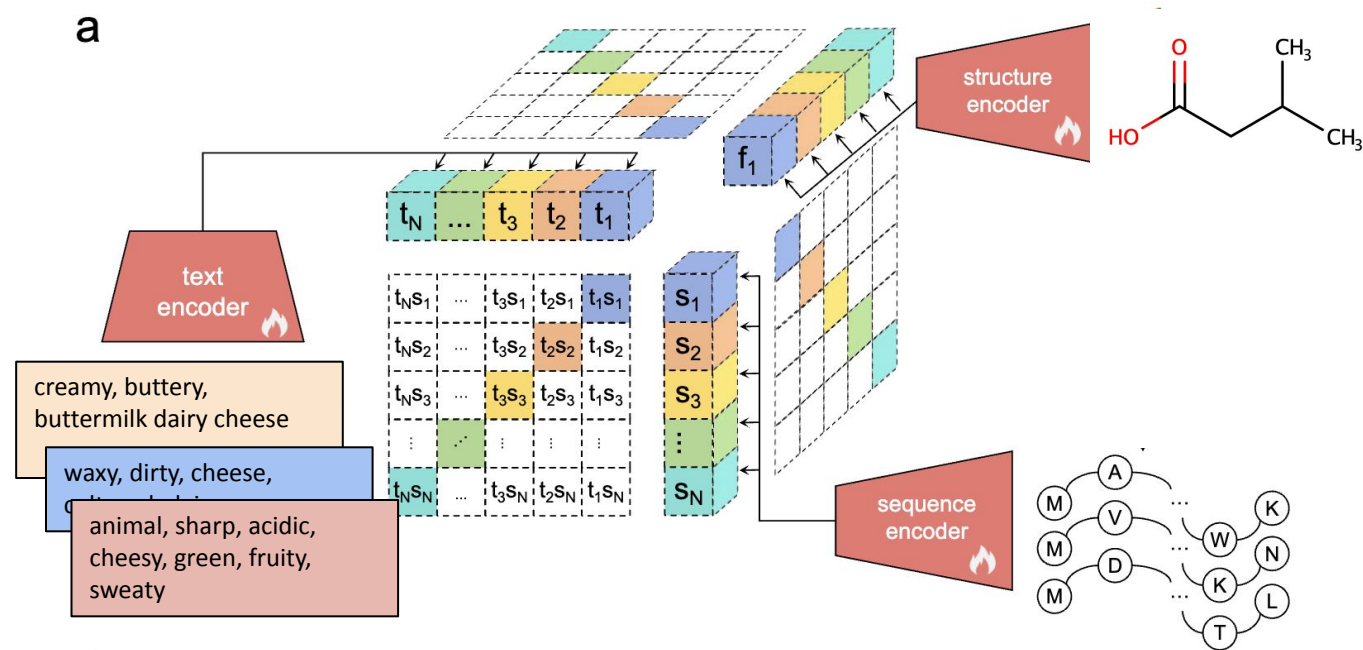
Protein: [ESM-2](#) (148M)

Text: [BiomedBERT](#) (109M)

SM: [MolFormer-XL](#) (45M)

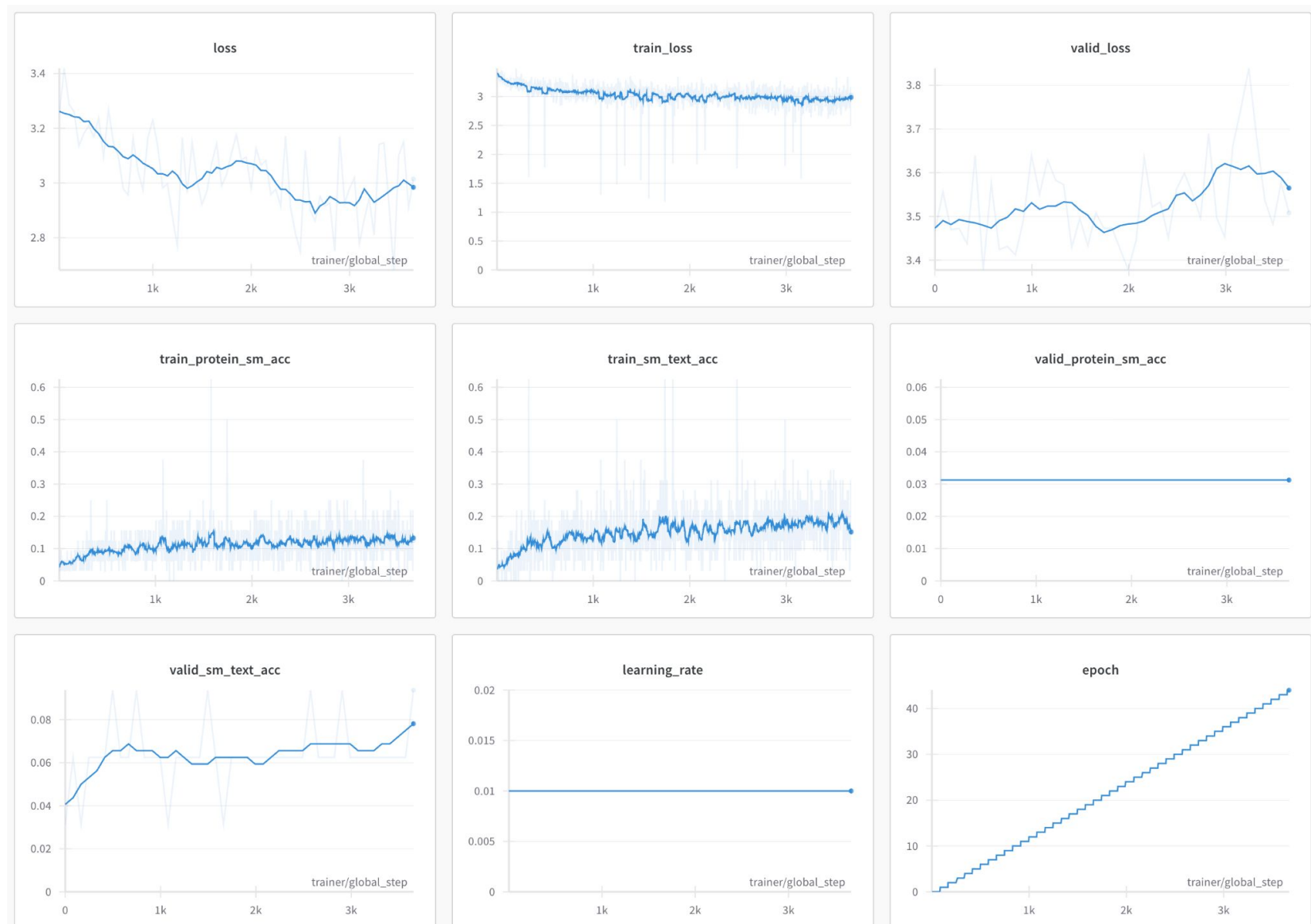
trained via trimodal CLIP-loss

(inspired by [ProTrek](#))

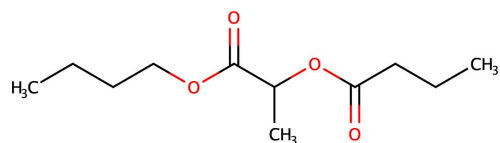


# Training

Loss going down,  
sort of







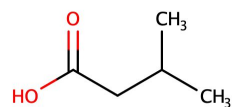
Butyl butyryl lactate

# Odor Description

creamy, buttery,  
buttermilk dairy cheese

# DiffDock Binding Score

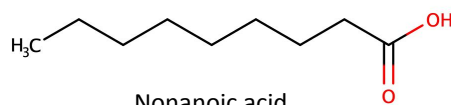
**-1.09**



Isovaleric acid

sour, sweaty, cheesy,  
tropical

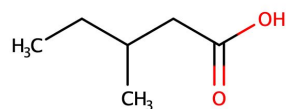
**-0.492**



Nonanoic acid

waxy, dirty, cheese,  
cultured, dairy

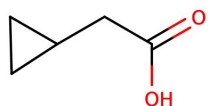
**-0.658**



3-methylpentenoic acid

animal, sharp, acidic,  
cheesy, green, fruity,  
sweaty

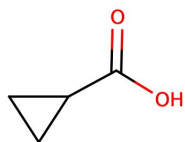
**-1.226**



2-cyclopropylacetic acid

????

**-0.21**

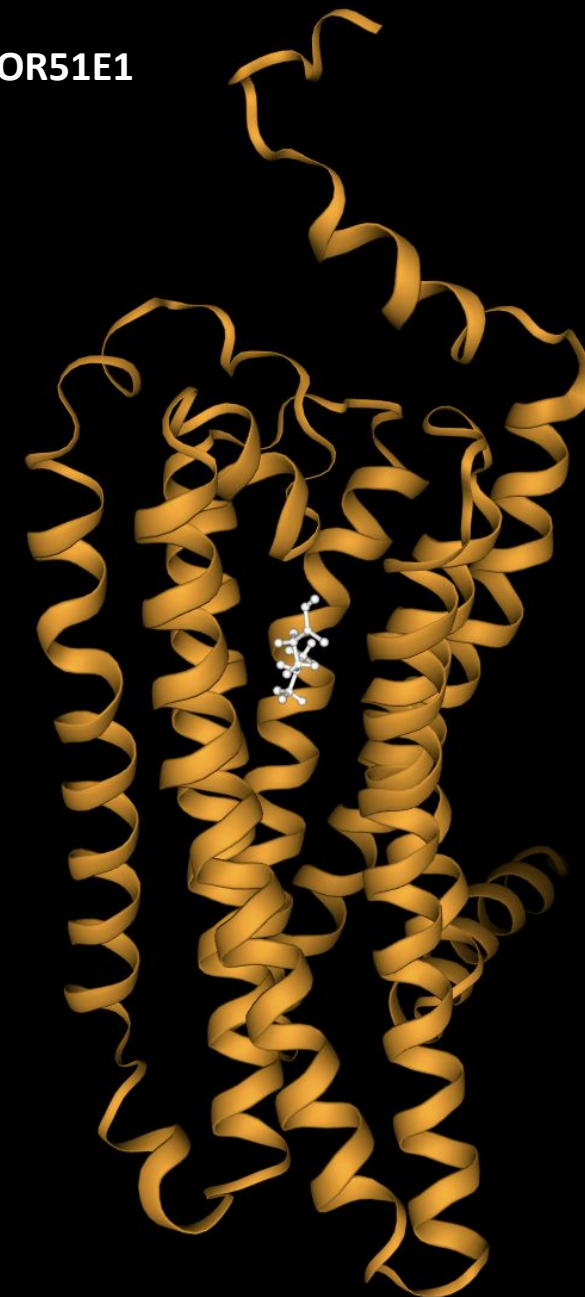


Cyclopropanecarboxylic acid

????

**0.312**

**OR51E1**



## **Future Applications?**

Flavor and Fragrance molecule design

Design of drugs for ectopic olfactory receptor targets

Flavor/Fragrance Digitization and 'Compression': a 'flavor printer' to go with your 3D food printer

Personalized molecular cocktail of flavor ligands based on genetic screening of e.g. tumor cells



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