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Supplementary Materials for

Functional odor classification through a medicinal chemistry approach

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This PDF file includes:

Supplementary Materials

		OSNs responding to					
		[1]	**[2]**	**[3]**	**[4]**	**[5]**	**[6]**
Co-activated by	**[1]**		**88.2**	78.9	74.4	77.4	78.3
	[2]	**85.6**		61.9	74.0	79.5	82.2
	[3]	62.2	50.3		66.5	82.1	83.3
	[4]	73.5	75.4	83.4		82.0	83.3
	[5]	50.0	52.9	67.2	66.5		**88.7**
	[6]	46.5	50.3	62.8	49.9	**81.5**	

fig. S1. OSNs co-activation Table. Numbers represent the percentage of OSNs responding to an odorant that are co-activated by another odorant of the panel. Green boxes represent the reverse ester pairs **[1]**, **[2]** and **[5]**, **[6]**. Note that reverse esters pairs show the highest reciprocal co-activation level.

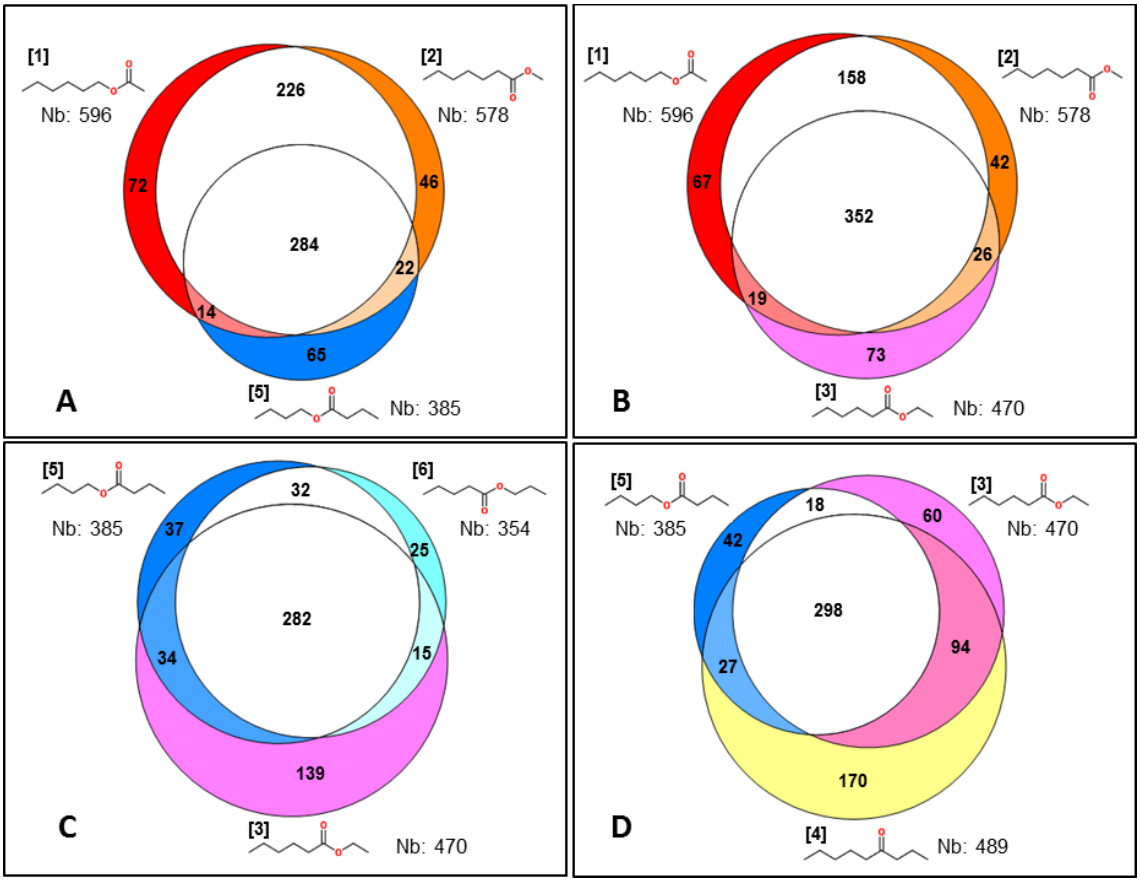

fig. S2. Venn-diagram representation of the overlapping activation of OSNs by esters. Responding OSNs were counted and converted into surface area for each response combination using the eulerAPE free software (*32*). The number of OSNs responding with that pattern is indicated in that sector. In panels (**A**) and (**B**) we compare the terminal esters ester **[1]** and **[2]** (its reverse ester) with the medial esters **[5]** and **[3]** respectively. Here it is readily apparent that the terminal esters have greater overlap with each other than with either of the medial esters. Similarly, in panel (**C**) we compare the medial ester **[5]** and its reverse ester **[6]** which overlap more with each other than with the seemingly similar medial ester **[3]**, which has a large number of cells that respond only to it. In panel (**D**) the ketone, originally chosen as an outsider non-ester odor, shows the expected large number of individual responses. But unexpectedly there is a significant overlap with the medial esters **[5]** and **[3]**.All odorants were tested at 30µM. 4523 viable OSNs were screened. **[1]**: red, **[2]**: orange, **[3]**: pink, **[4]**: yellow, **[5]**: dark blue, **[6]**: light blue, Nb: Number of OSNs responding to the given odorant.

Repetition one

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Subject 1	1	1	1	0	0	0	0
Subject 1	0	0	0	0	0	0	1
Subject 2	0	0	0	0	1	1	1
Subject 2	0	1	0	1	0	0	0
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Subject 7	0	0	0	0	1	1	0
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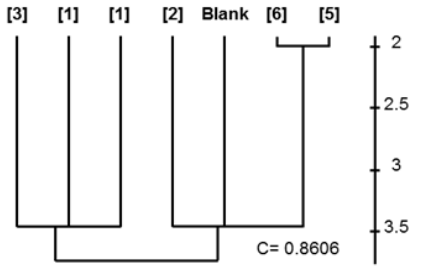

Repetition two

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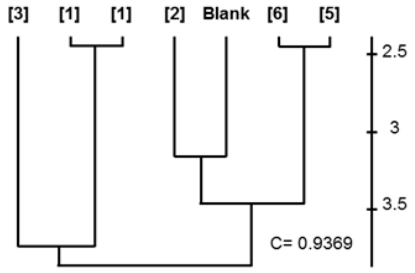

Repetition three

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Subject 2	1	1	0	0	0	0	0
Subject 2	0	0	1	1	0	0	0
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Subject 4	0	0	1	0	1	1	1
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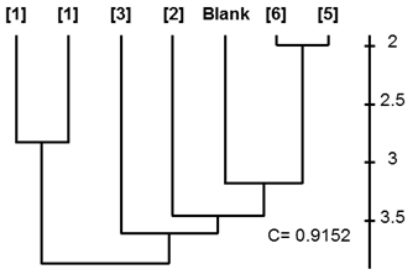

fig. S3. Human olfactory discrimination test repetitions. Odorant classification binary matrices of 30 µM odorant solutions by 11 human subjects over three iterations (i.e. Blue, Red, and Yellow). (1)= similar, (0)=different. Cluster analysis of each repetition is reported below its matrix. *C= Cophenetic correlation coefficient.

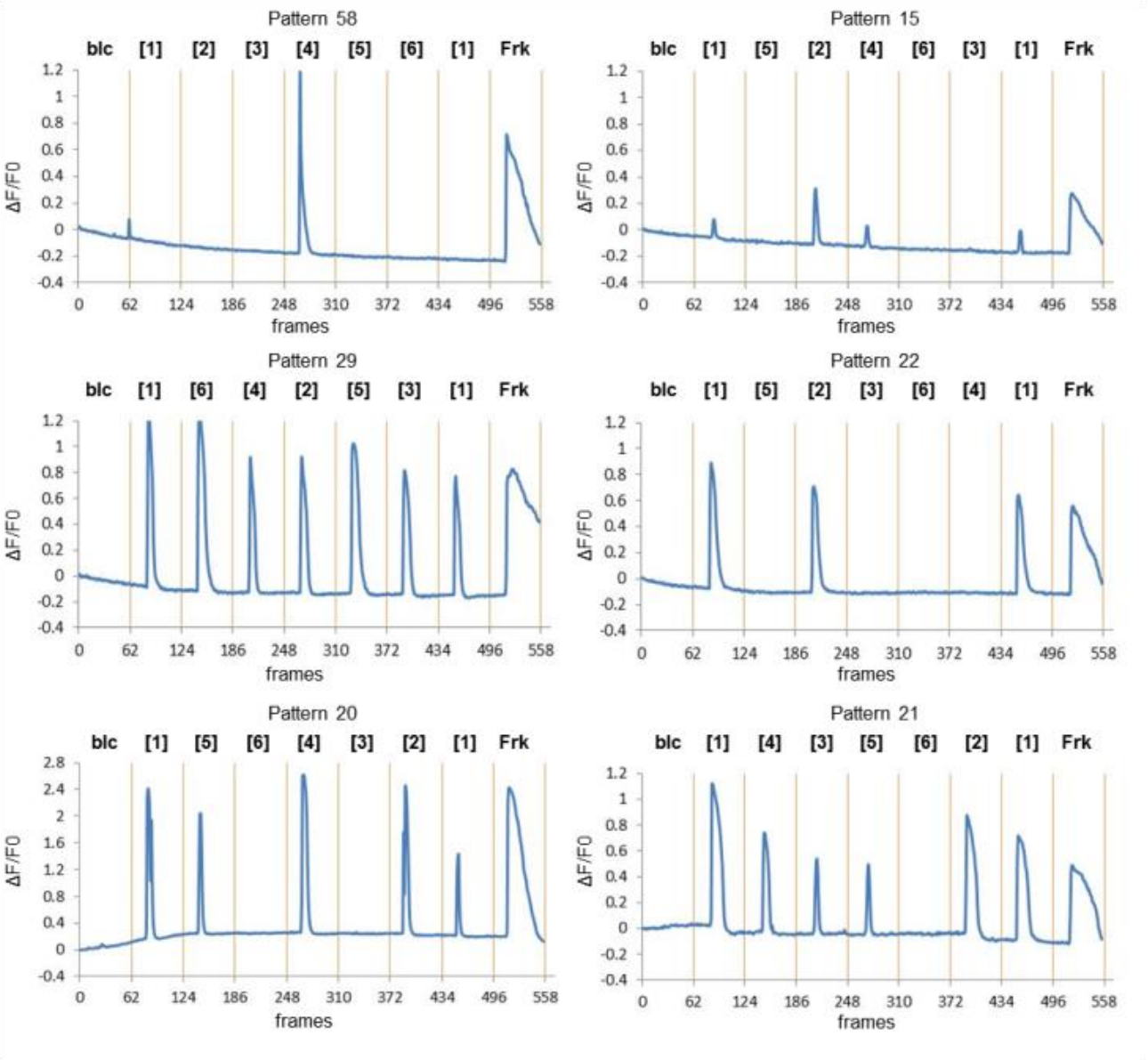

fig. S4. Examples of OSNs Ca^{2+} responses to the Odorant Panel. ΔF/F0 intensity changes of six different OSNs in response to odorant stimulations. Each trace represents a different response pattern including the most highly observed pattern (Pattern 29: 246 OSNs) and one of the least observed patterns (Pattern 20: one OSN), as reported in Fig. 1. **blc**: DMSO solvent only, **Frk** : forskolin.

table S1. Top 20 e-Dragon descriptors describing distances between the esters. List of the 20 e-Dragon molecular descriptors that best recapitulate the biology centered classification of the terminal ester cluster**[1]** and **[2]**, and the medial ester cluster **[3]**, **[5]**,and **[6]** based on their distance matrix Spearman's correlation factor. The ketone **[4]** was excluded from this analysis.

name	Full name	id	rho	Descriptor Type
'Whetm'	Wiener-type index from mass weighted distance matrix	86	0.99	topological descriptors
'Whete'	Wiener-type index from electronegativity weighted distance matrix	88	0.99	topological descriptors
'Jhete'	Balaban-type index from electronegativity weighted distance matrix	94	0.99	topological descriptors
'X3Av'	average valence connectivity index chi-3	236	0.99	connectivity indices
'Eig1Z'	Leading eigenvalue from Z weighted distance matrix (Barysz matrix)	584	0.99	eigenvalue-based indices
'Eig1m'	Leading eigenvalue from mass weighted distance matrix	585	0.99	eigenvalue-based indices
'Eig1e'	Leading eigenvalue from electronegativity weighted distance matrix	587	0.99	eigenvalue-based indices
'AEigZ'	Absolute eigenvalue sum from Z weighted distance matrix (Barysz matrix)	594	0.99	eigenvalue-based indices
'AEigm'	Absolute eigenvalue sum from mass weighted distance matrix	595	0.99	eigenvalue-based indices
'AEige'	Absolute eigenvalue sum from electronegativity weighted distance matrix	597	0.99	eigenvalue-based indices
'DELS'	molecular electrotopological variation	98	0.98	topological descriptors
'DISPm'	d COMMA2 value / weighted by atomic masses	690	0.98	geometrical descriptor
'HTm'	H total index / weighted by atomic masses	1184	0.98	GETAWAY descriptors
'Jhetm'	Balaban-type index from mass weighted distance matrix	92	0.98	topological descriptors
'Dm'	D total accessibility index / weighted by atomic masses	1140	0.98	WHIM descriptors
'H0m'	H autocorrelation of lag 0 / weighted by atomic masses	1175	0.98	GETAWAY descriptors
'WhetZ'	Wiener-type index from Z weighted distance matrix (Barysz matrix)	85	0.96	topological descriptors
'H1m'	H autocorrelation of lag 1 / weighted by atomic masses	1176	0.95	GETAWAY descriptors
'HATSm'	leverage-weighted total index / weighted by atomic masses	1194	0.95	GETAWAY descriptors