

**实用生物信息技术期末总结交流报告会**

**Piezo1蛋白同源结构预测、功能探究及其激动剂  
Yoda1的对接模拟**

报告人：王泽仪 李媛媛 许杞钦

2021年1月23日

## 小组成员

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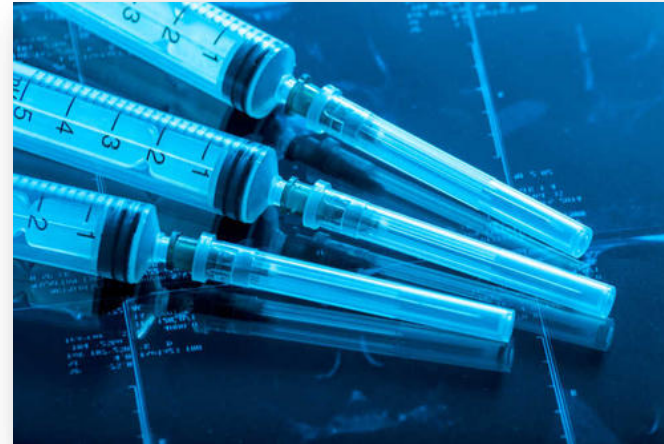
编号	姓名	学院	导师	研究方向
G14A	王泽仪	深研院	周强	神经退行性疾病与精神疾病
G14B	李媛媛	生科院	蒋争凡	天然免疫与肿瘤治疗
G14C	许杞钦	生科院	季雄	RNA聚合酶亚基调控的分子机理

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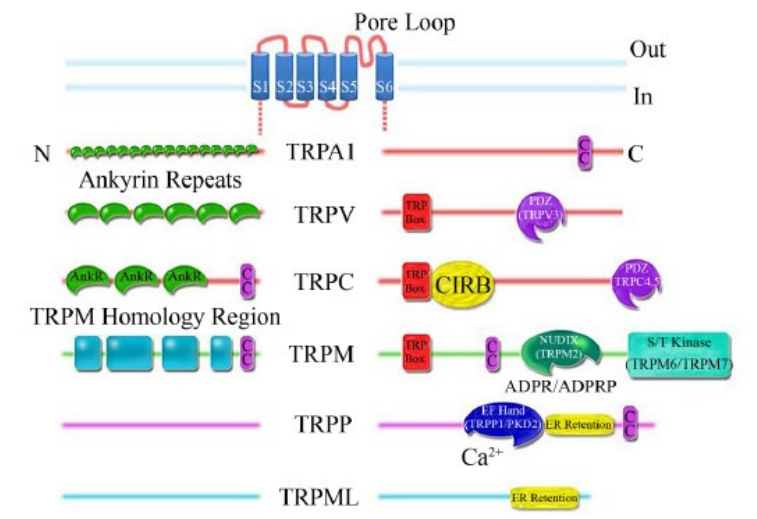
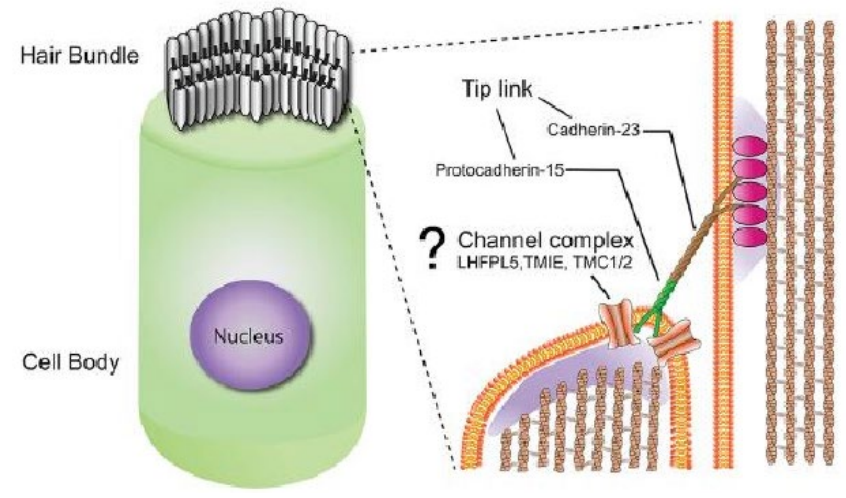
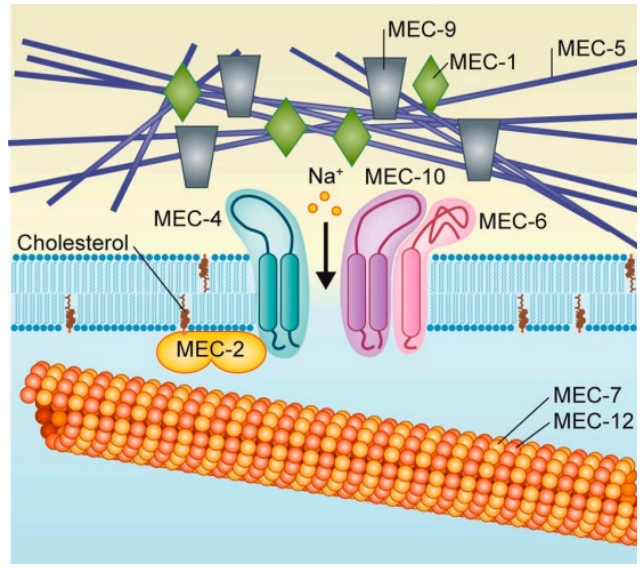
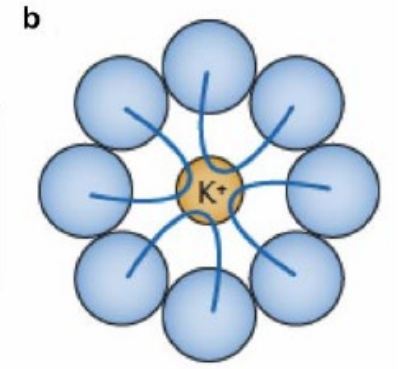
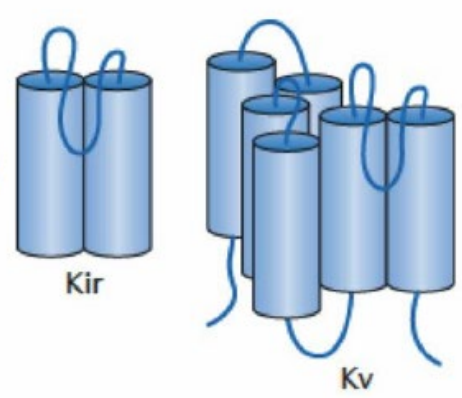
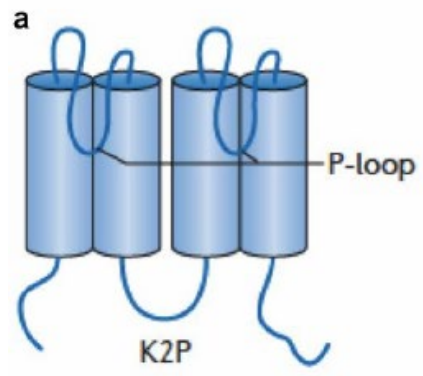
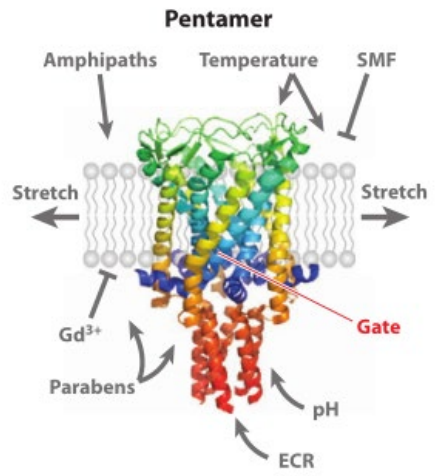
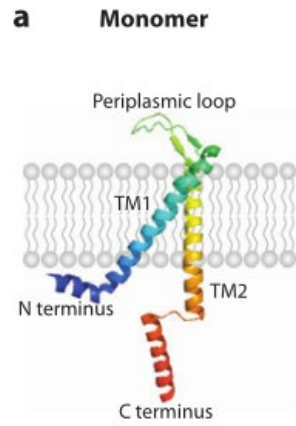
# CONTENT

- Background
- Structure prediction and functional analysis
- Molecular docking of Yoda1 and Piezo1

# Mechanical feelings are closely related to life activities

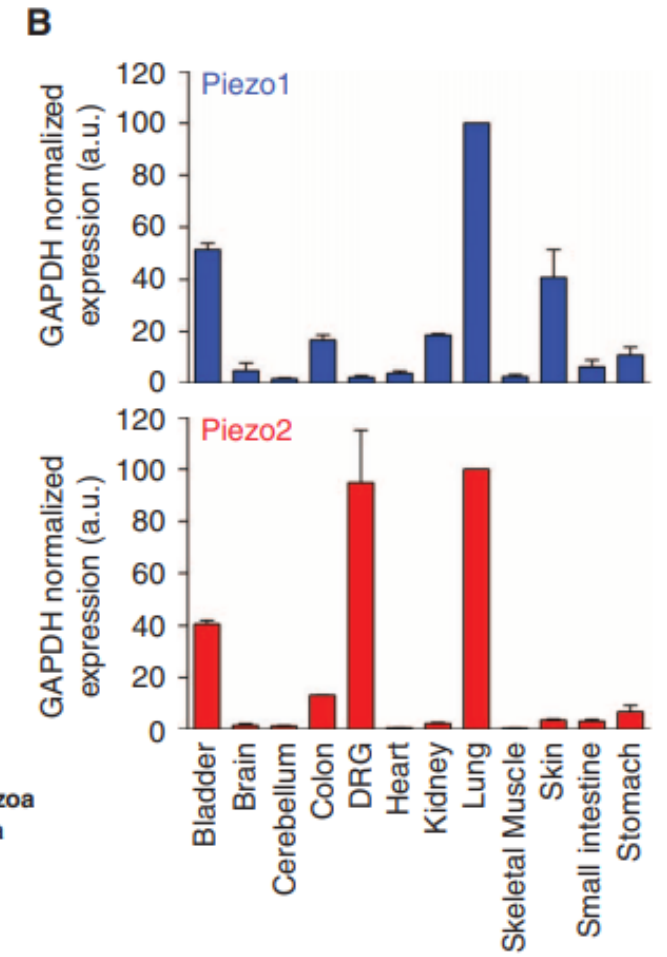
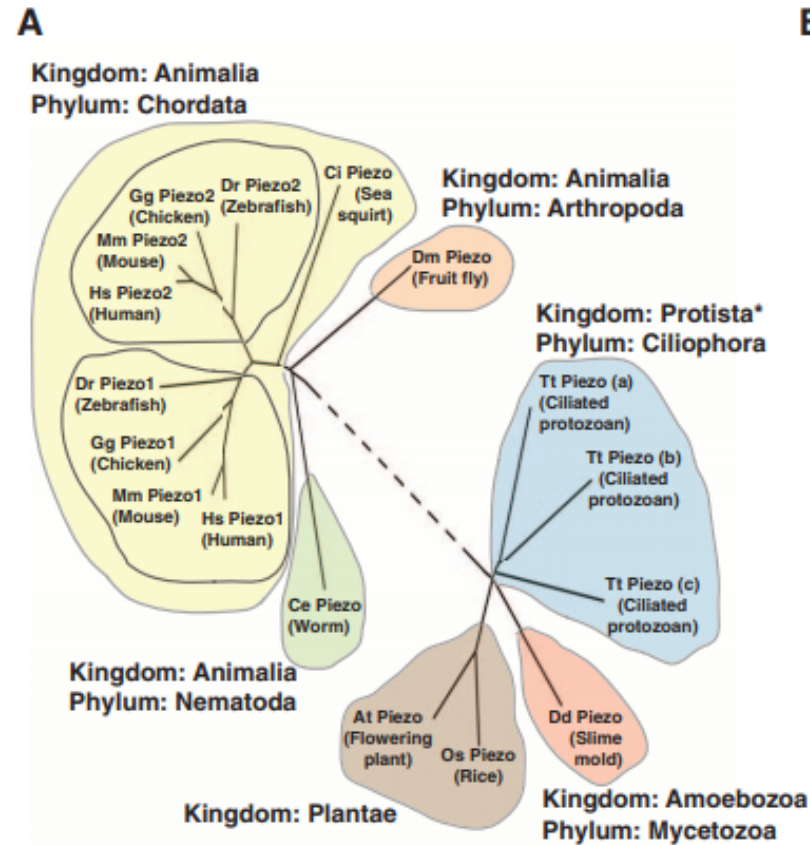
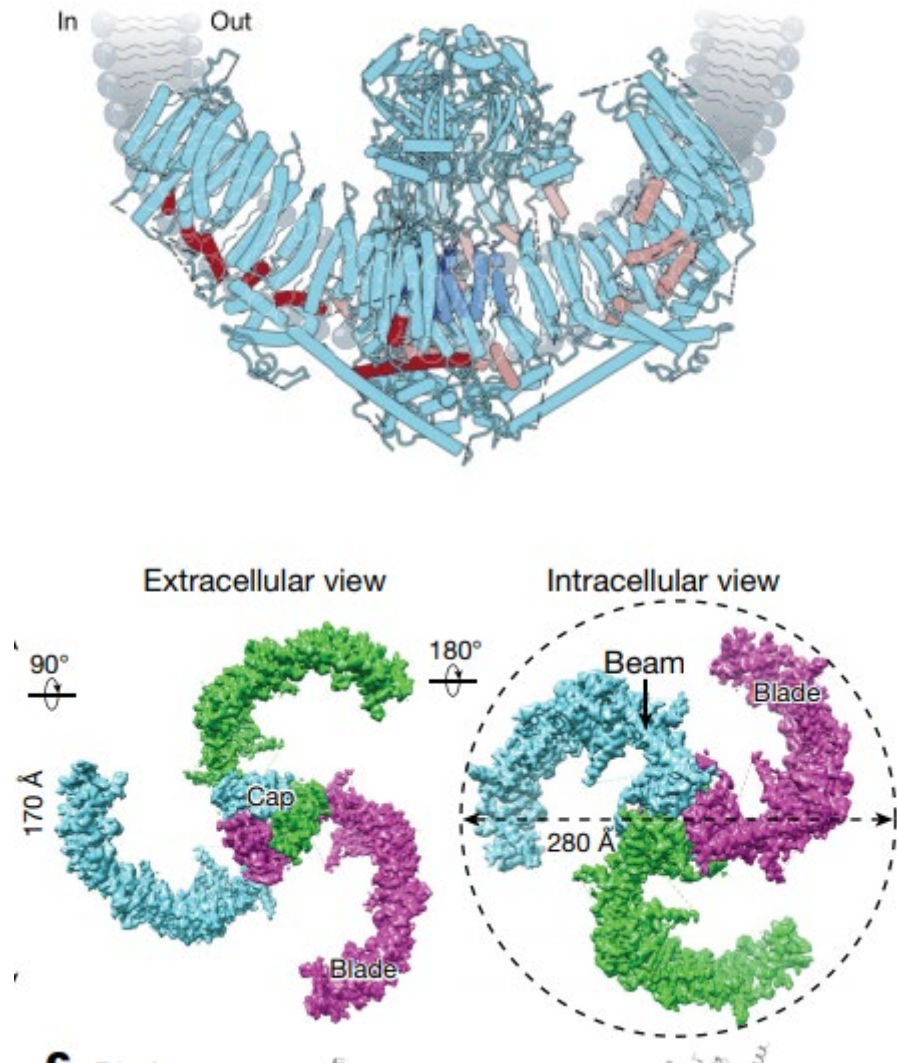


# Mechanosensory related molecules in different organisms



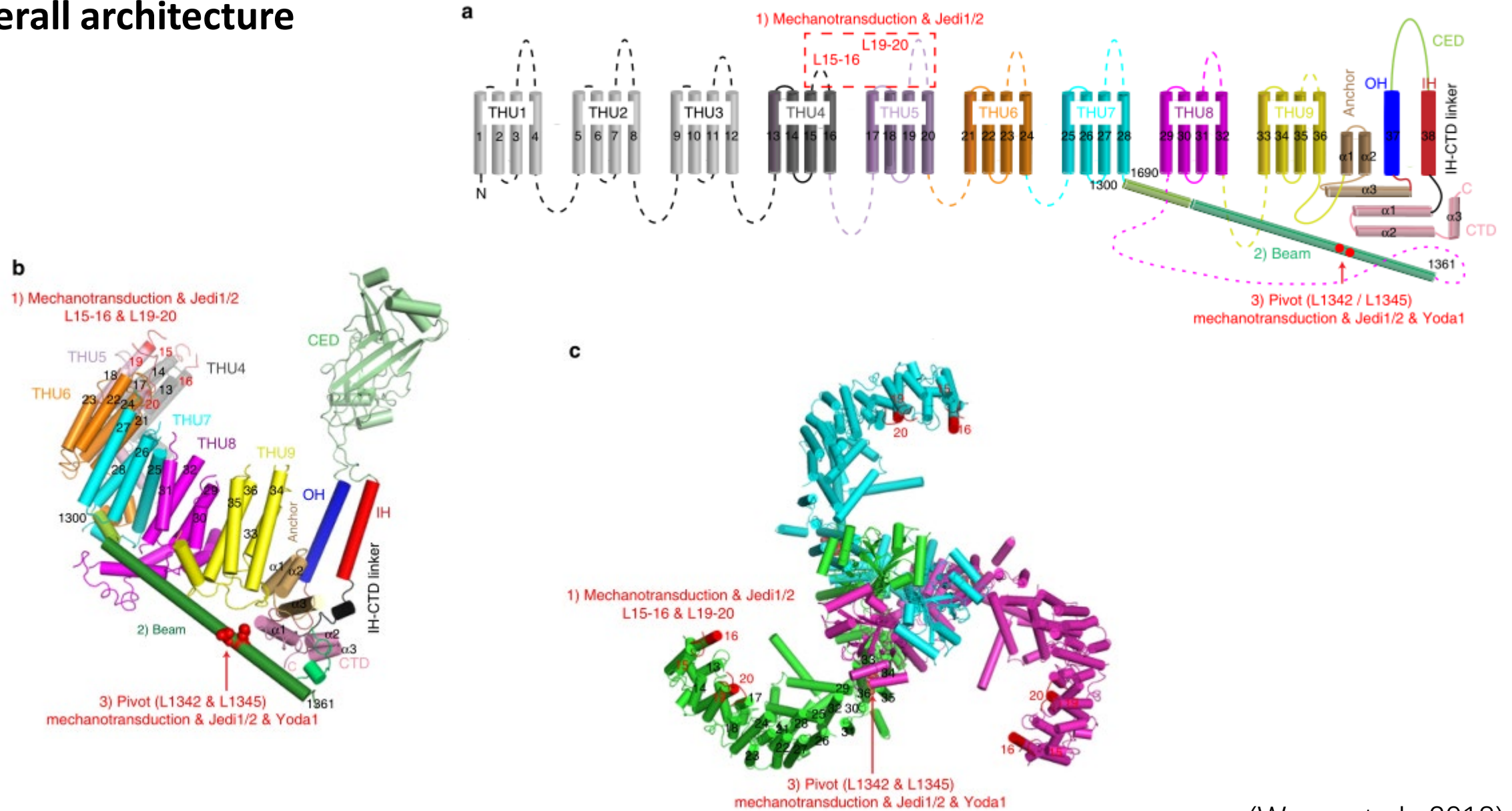
(Kung et al., 2010; Lumpkin et al., 2010)

# The first identified class of cationic mechanotransducers in mammals



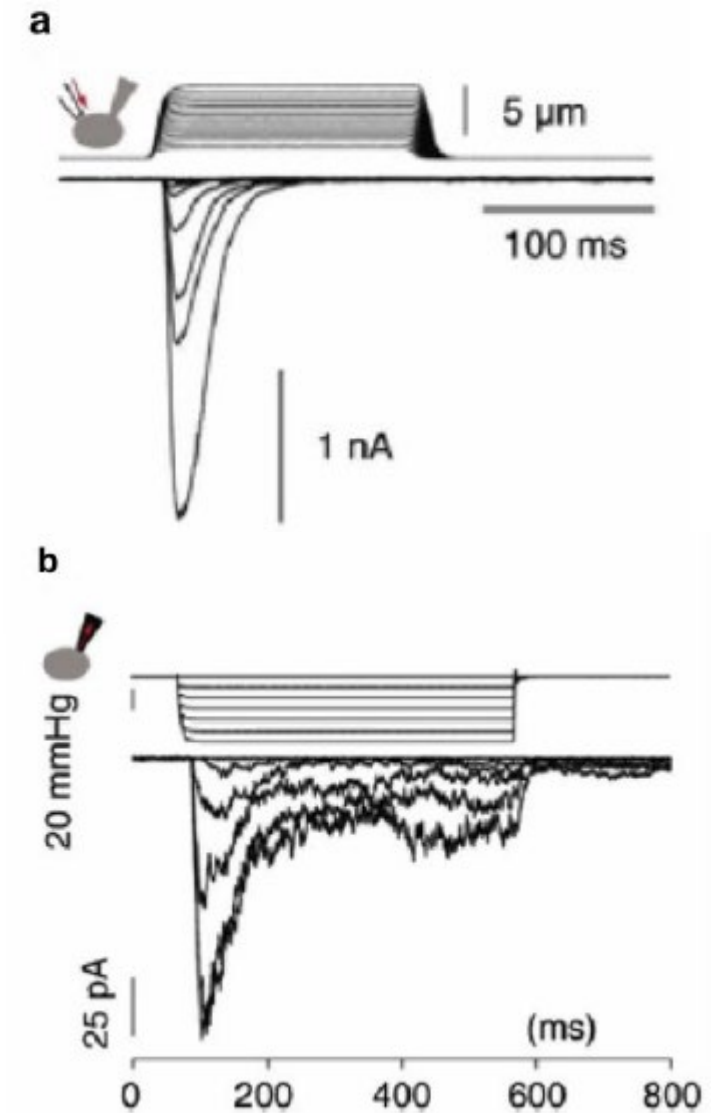
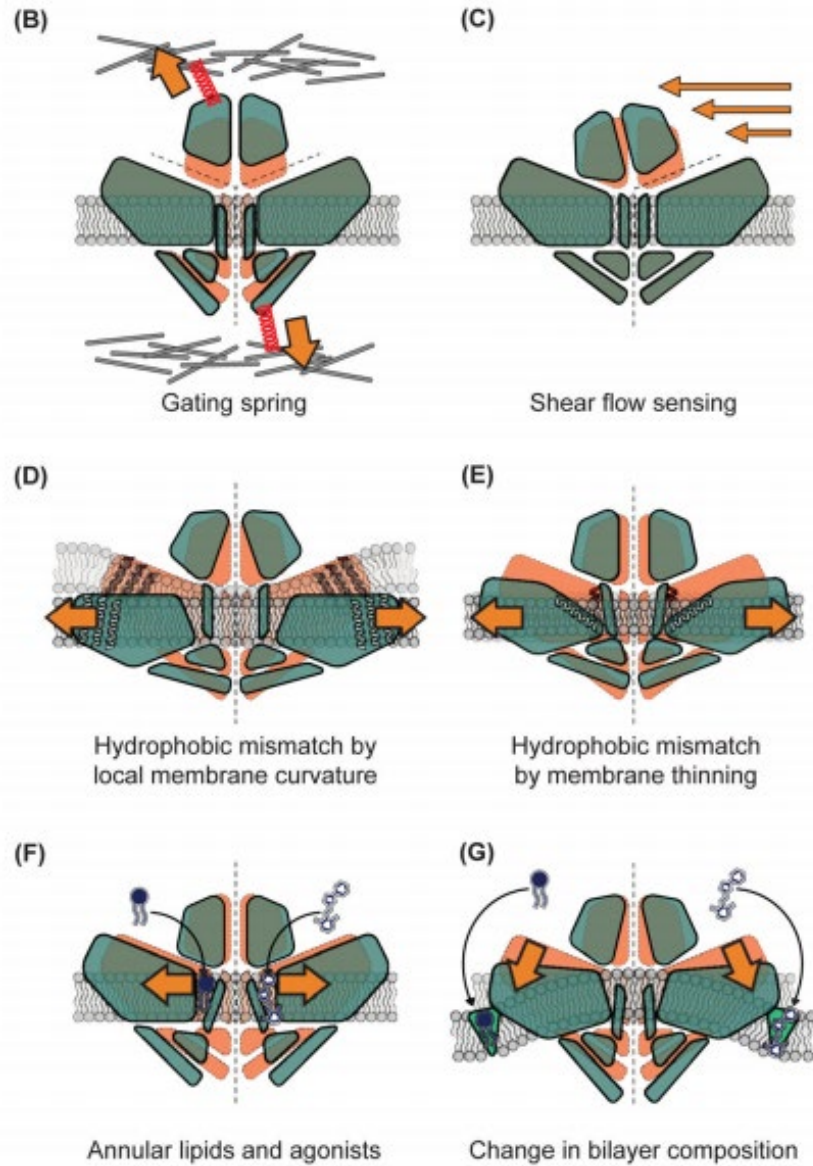
(Wang et al.,2019;Kefauver et al.,2020;Coste et al., 2010)

# Overall architecture



(Wang et al., 2018)

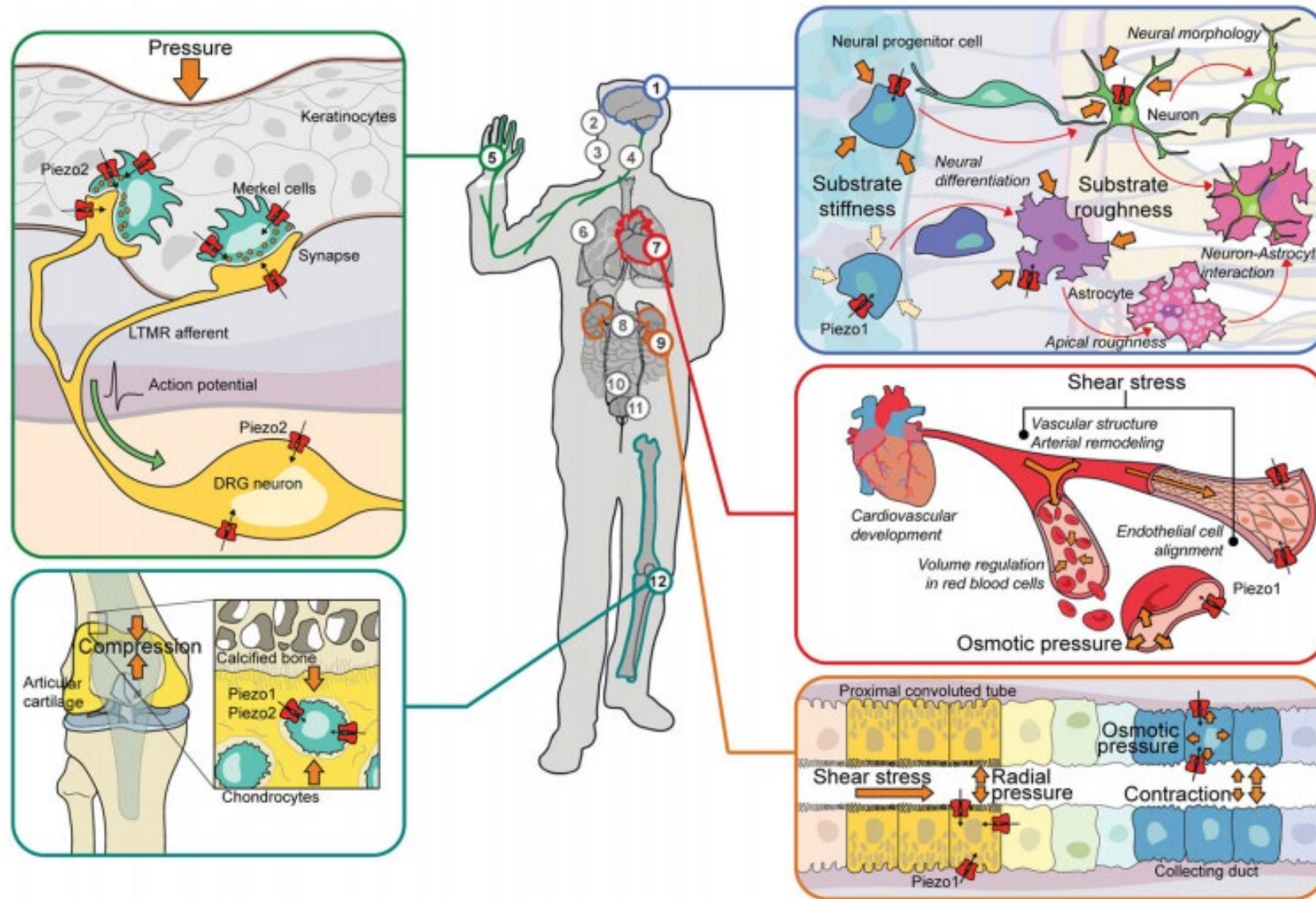
# Gating mechanism and electrophysiological properties



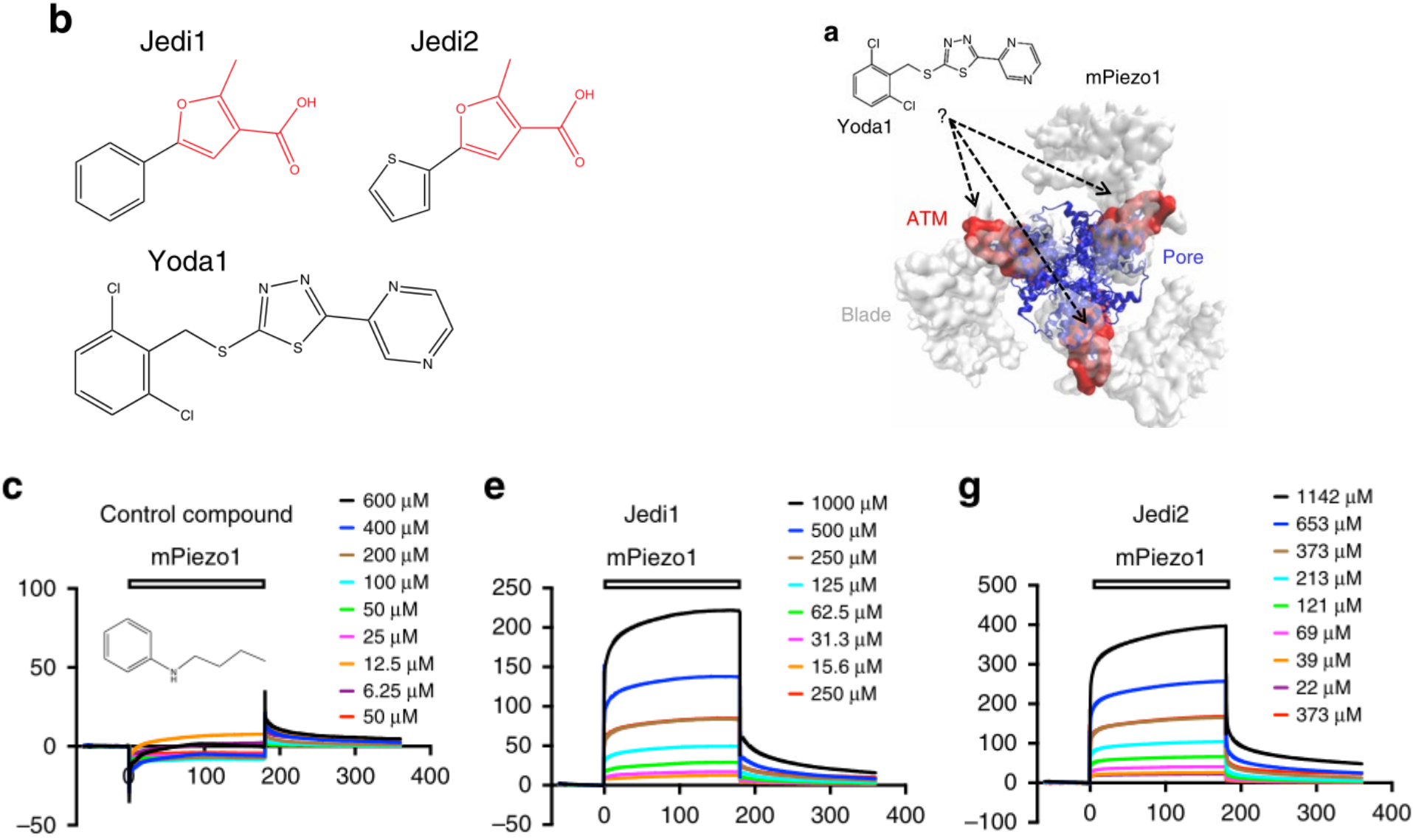
(Wu et al., 2017; Coste et al., 2010)



# Expression and physiological roles of Piezos



# Lacking of pharmacological tools and unclear mechanisms hamper researches of Piezo1

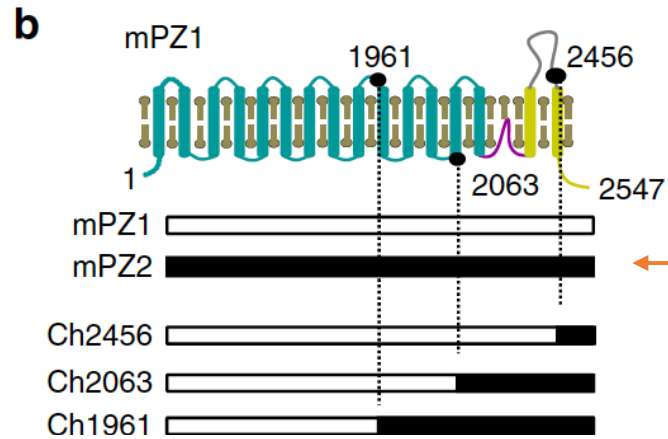


(Lacroix et al., 2018;Wang et al.,2018)

## **Research purposes**

- Structure prediction and functional analysis
- Molecular docking of Yoda1 and Piezo1

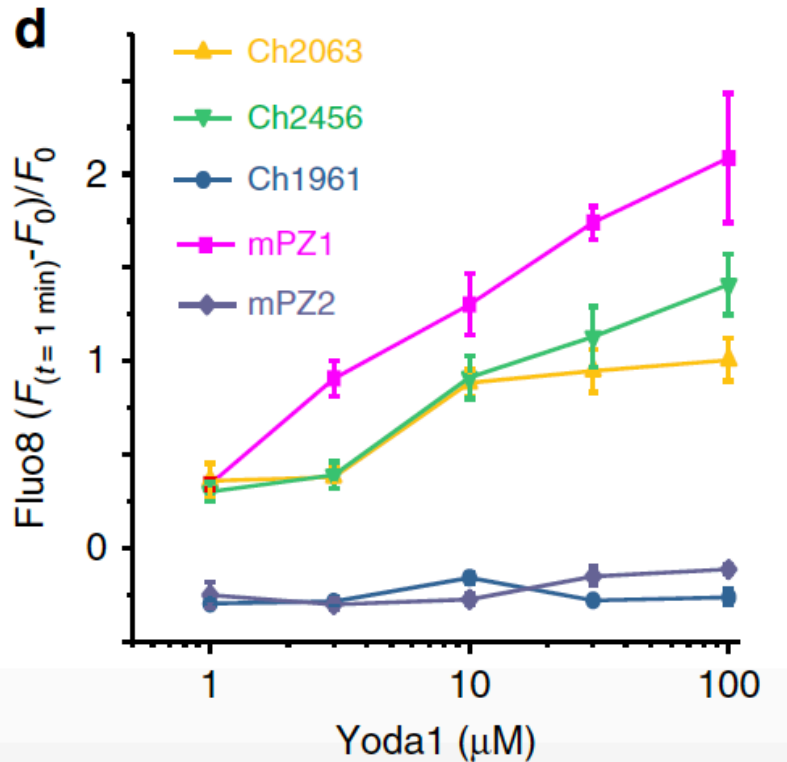
# Needle Piezo family in Mouse for alignment



No response to Yoda1

MATRIX	GAP_OPEN	GAP_EXTEND	END_GAP_PENALTY	END_GAP_OPEN	END_GAP_EXTEND
BLOSUM62	20	1.0	false	10	0.5

```
# Aligned_sequences: 2
# 1: PIEZ2_MOUSE
# 2: PIEZ1_MOUSE
# Matrix: EBLOSUM62
# Gap_penalty: 20.0
# Extend_penalty: 1.0
#
# Length: 2882
# Identity: 1189/2882 (41.3%)
# Similarity: 1633/2882 (56.7%)
# Gaps: 395/2882 (13.7%)
# Score: 5232.0
```





# Piezo1 (Mus musculus) blast in UniprotKB/Swiss-Prot

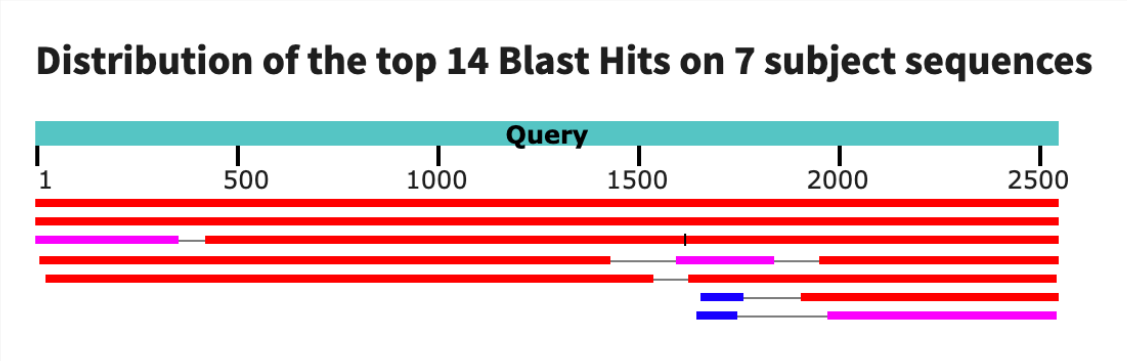
[Descriptions](#) | [Graphic Summary](#) | [Alignments](#) | [Taxonomy](#)

**Sequences producing significant alignments** Download  Select columns  100

select all *7 sequences selected*

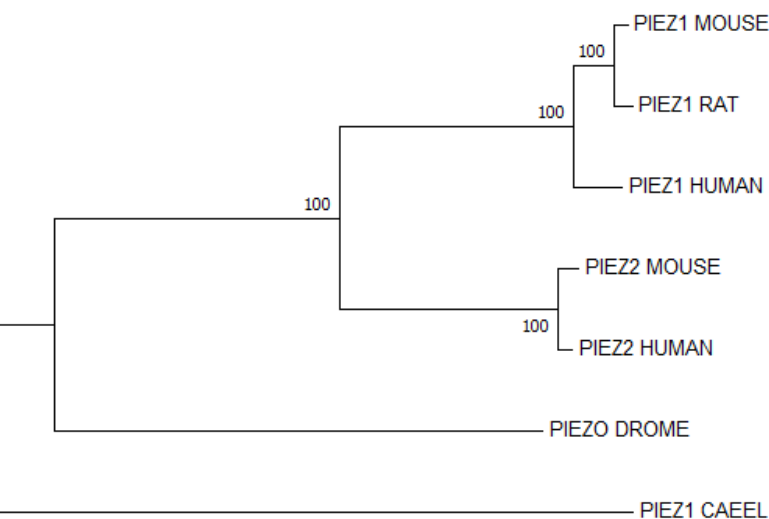
[GenPept](#) | [Graphics](#) | [Distance tree of results](#) | [Multiple alignment](#) |  [MSA Viewer](#)

	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel component 1; AltName: Full=Membrane protein ind...	<a href="#">Rattus norvegicus</a>	4627	4627	100%	0.0	93.49%	2535	<a href="#">Q0KL00.3</a>
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel component 1; AltName: Full=Membrane protein ind...	<a href="#">Homo sapiens</a>	3896	3896	100%	0.0	80.19%	2521	<a href="#">Q92508.4</a>
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel component 2; AltName: Full=Protein FAM38B [Hom...	<a href="#">Homo sapiens</a>	1023	2197	97%	0.0	43.35%	2752	<a href="#">Q9H515.2</a>
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel component [Drosophila melanogaster]	<a href="#">Drosophila mela...</a>	459	1023	88%	7e-129	26.87%	2551	<a href="#">M9MSG8.1</a>
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel component 1 [Caenorhabditis elegans]	<a href="#">Caenorhabditis...</a>	451	750	95%	1e-126	31.20%	2442	<a href="#">A0A061ACU2.1</a>
<input checked="" type="checkbox"/>	RecName: Full=Protein PIEZO homolog [Dictyostelium discoideum]	<a href="#">Dictyostelium dis...</a>	222	269	29%	2e-56	25.55%	3080	<a href="#">Q54S52.1</a>
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel homolog [Arabidopsis thaliana]	<a href="#">Arabidopsis thali...</a>	196	239	26%	2e-48	27.30%	2462	<a href="#">F4IN58.1</a>

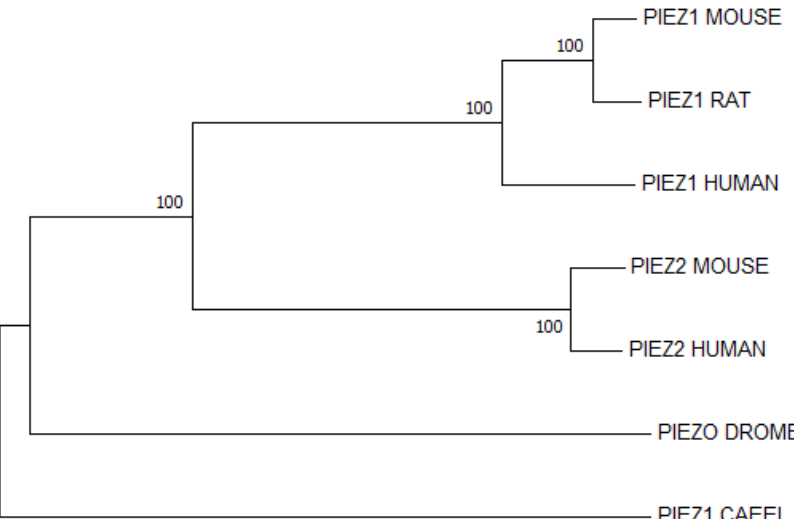




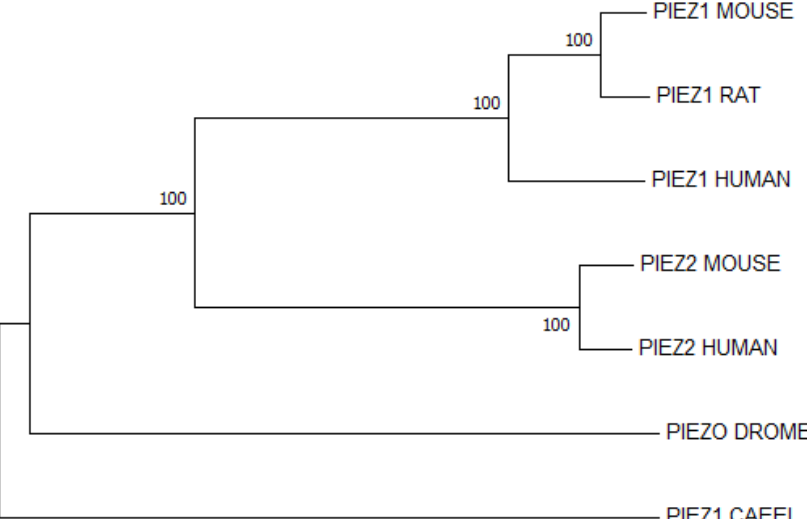
# Reviewed Piezo family in MEGA



Maximum Likelihood method



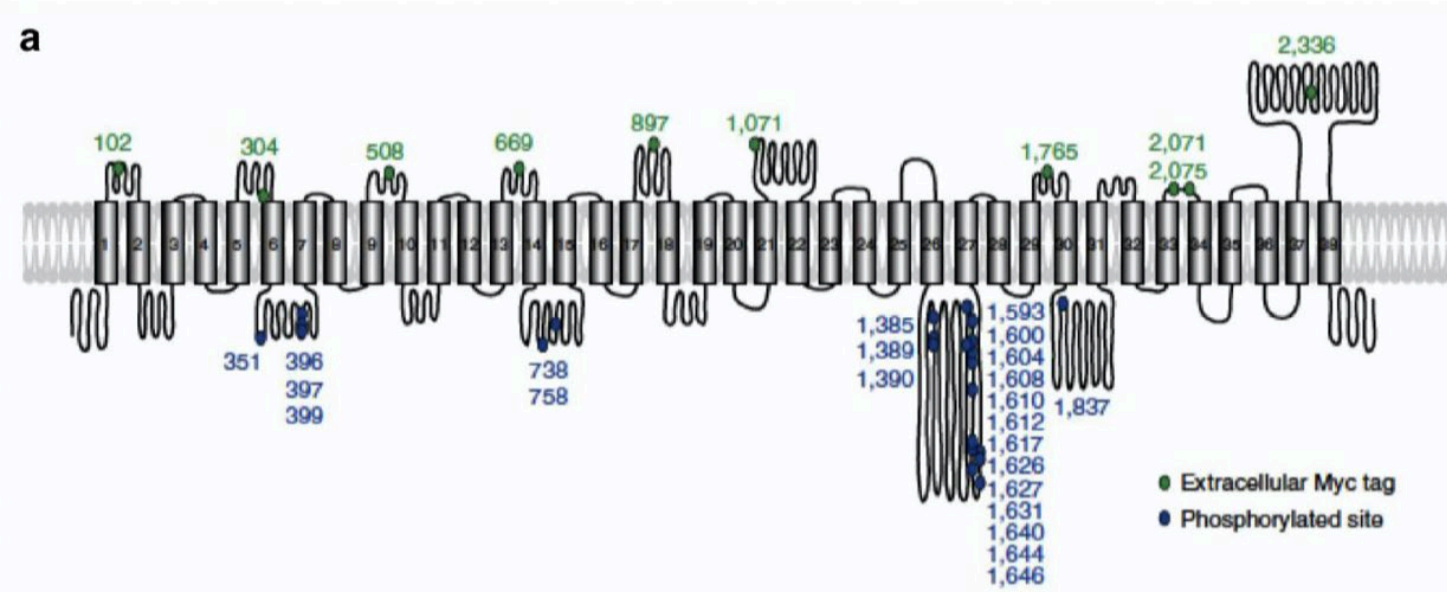
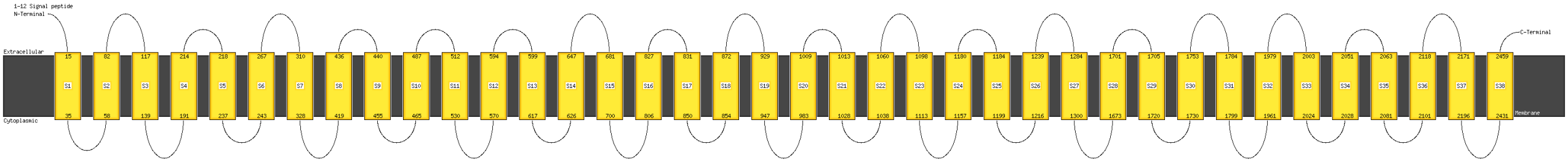
Neighbor-Joining method



Minimum Evolution method

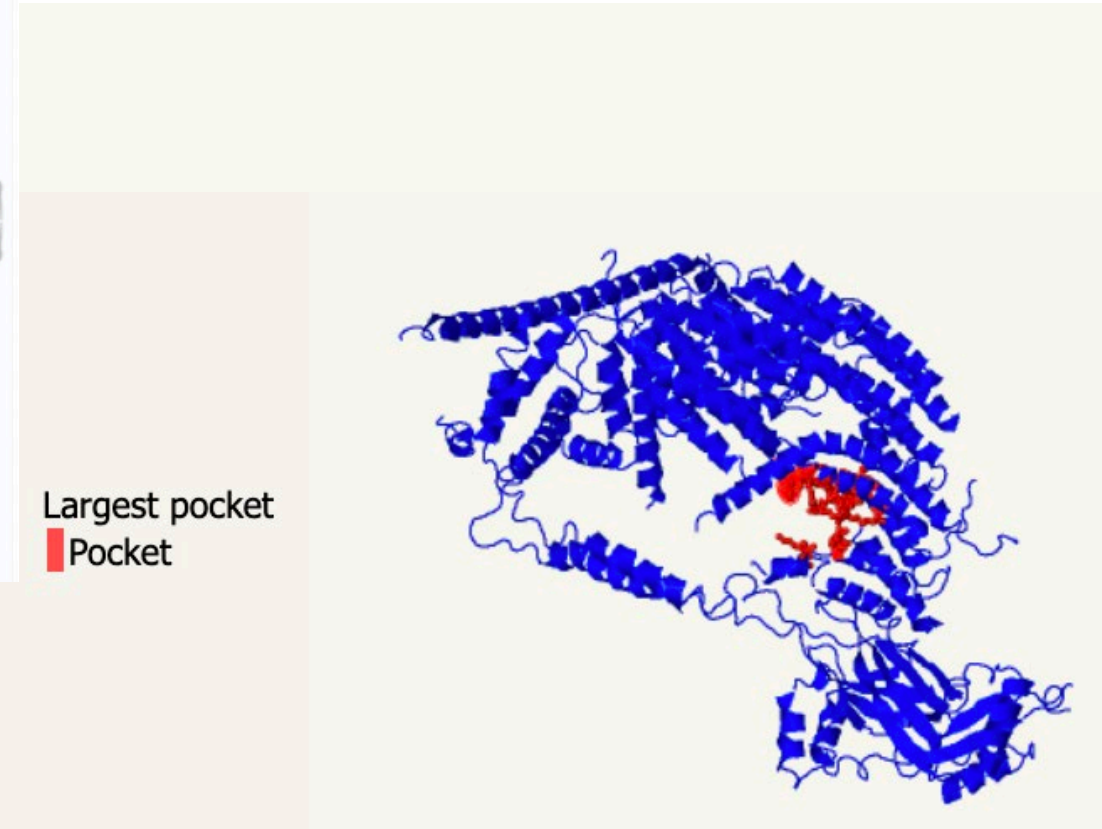


# Piezo1 (Homo sapien) predicted on Phyre2 web

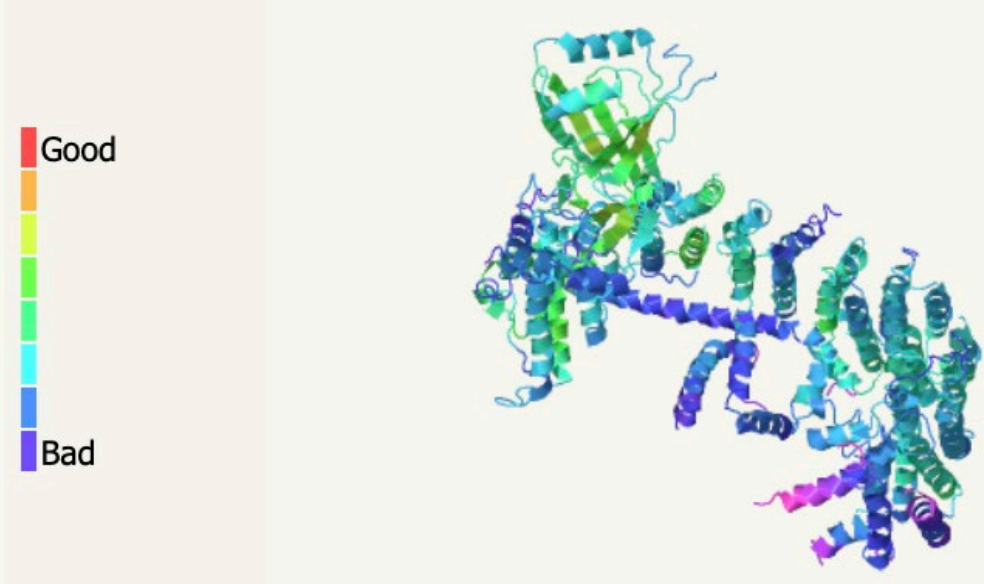
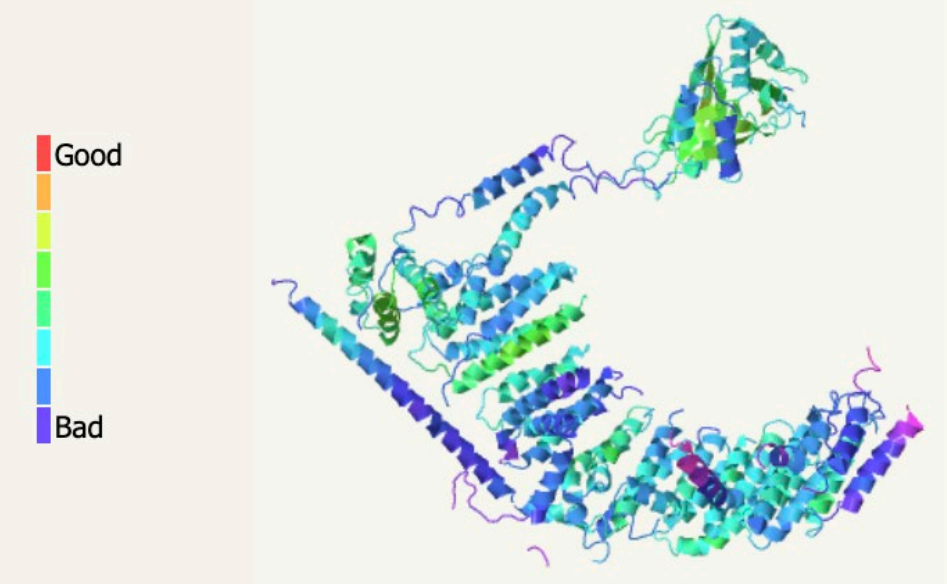


Piezo1\_Mouse

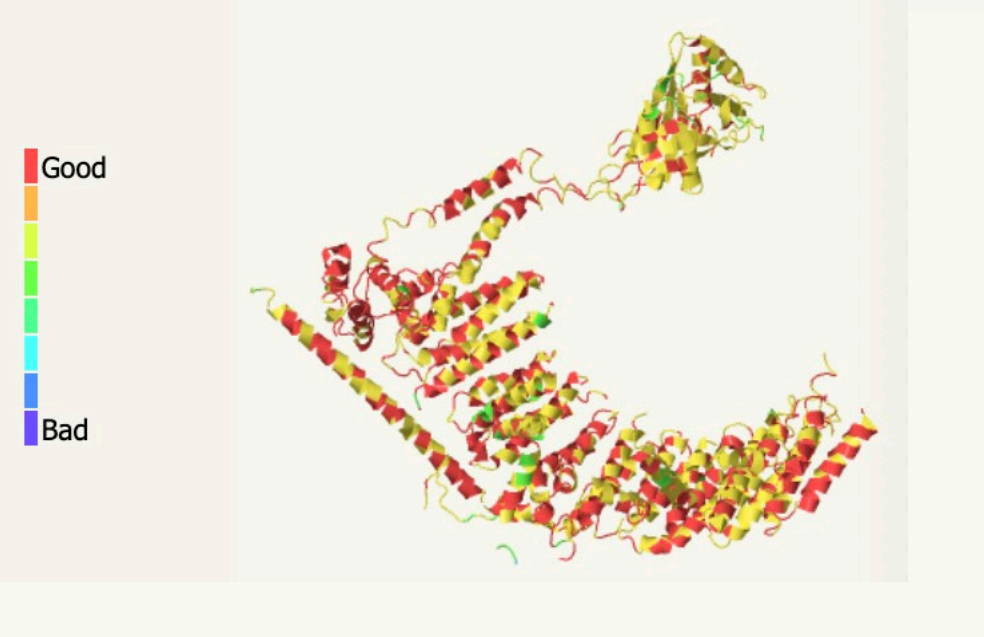
Coste et al., 2015



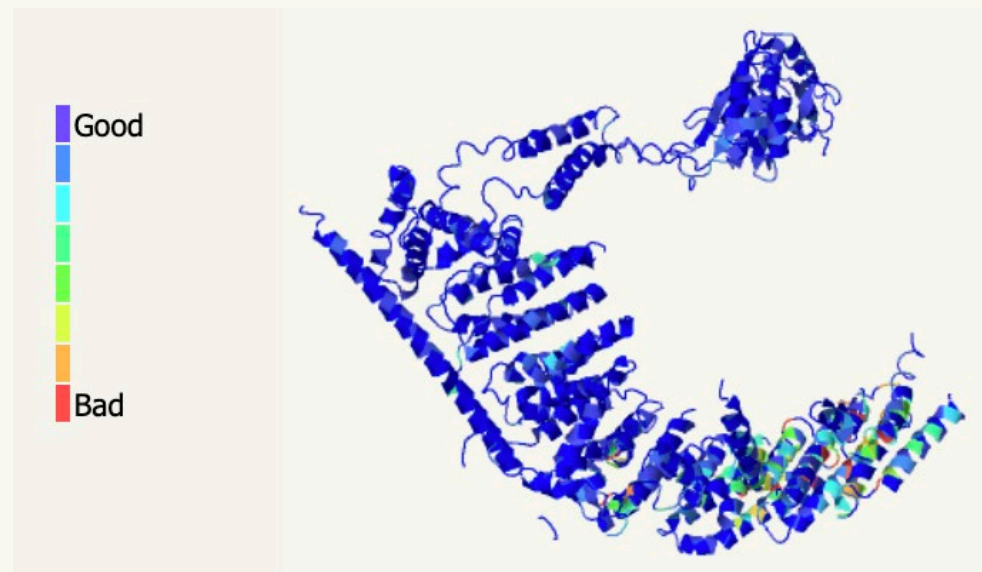
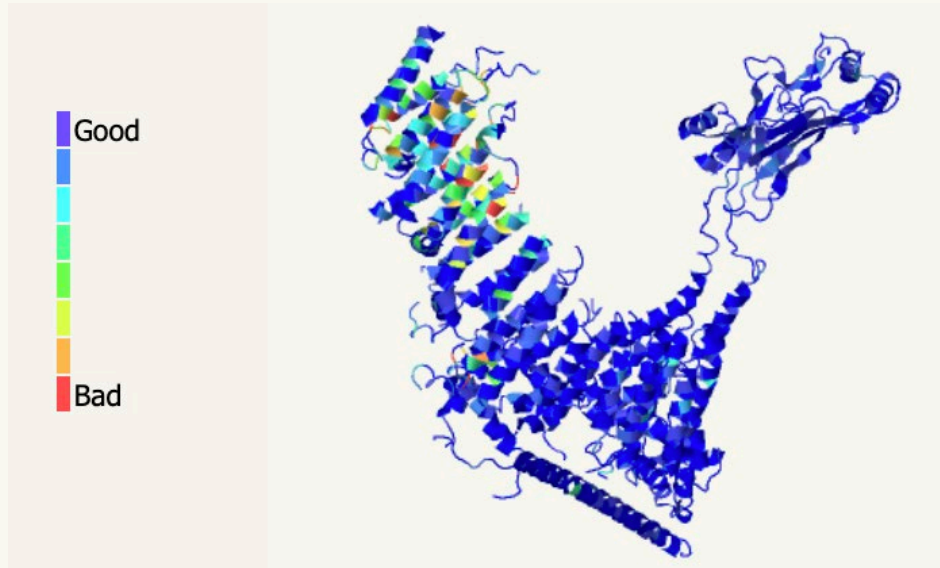
# ProQ2 quality assessment



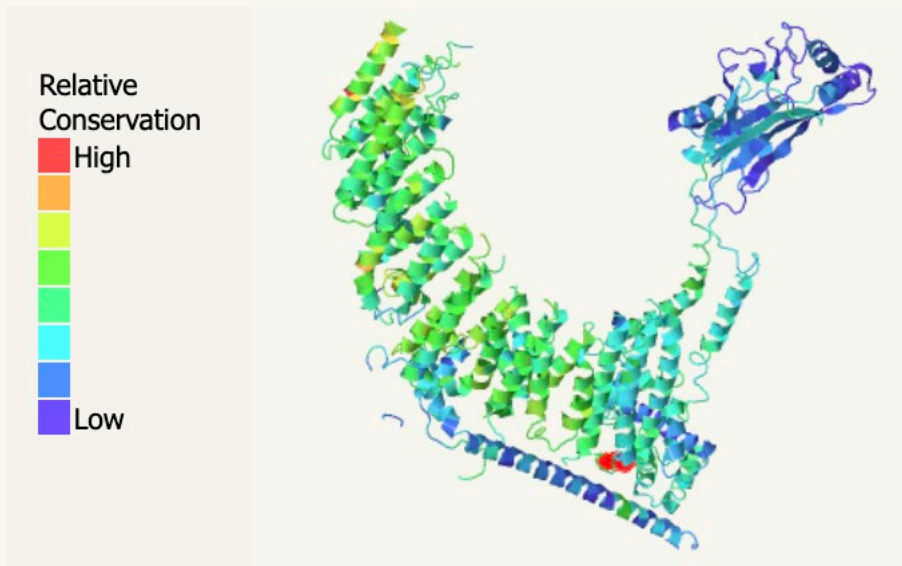
# Alignment Confidence



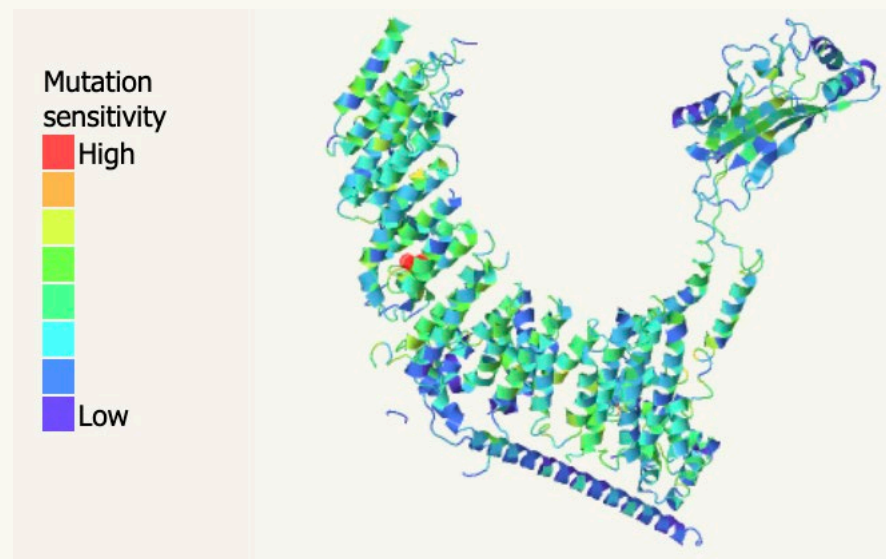
# Clash Analysis



# Conservation

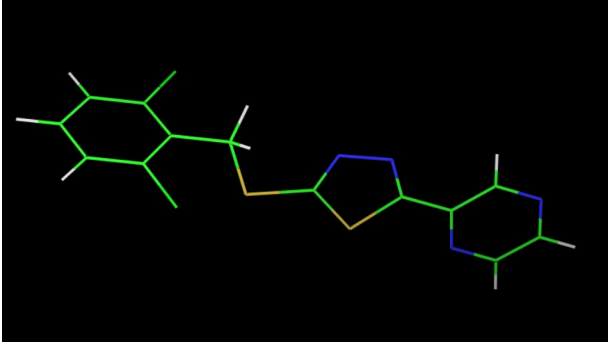
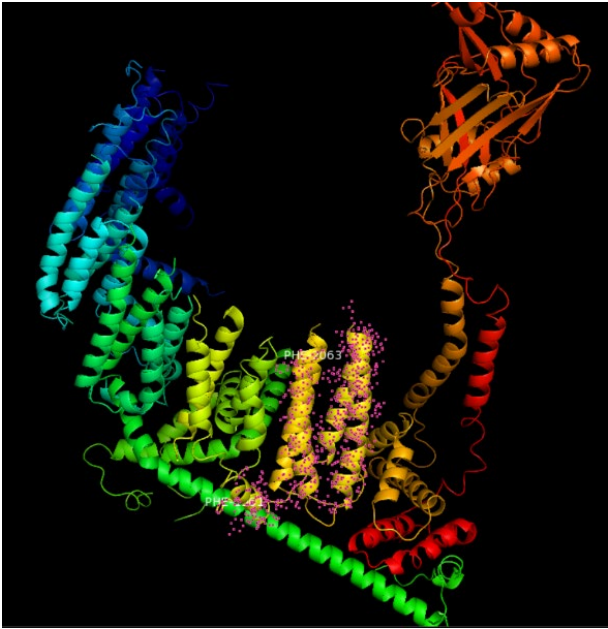
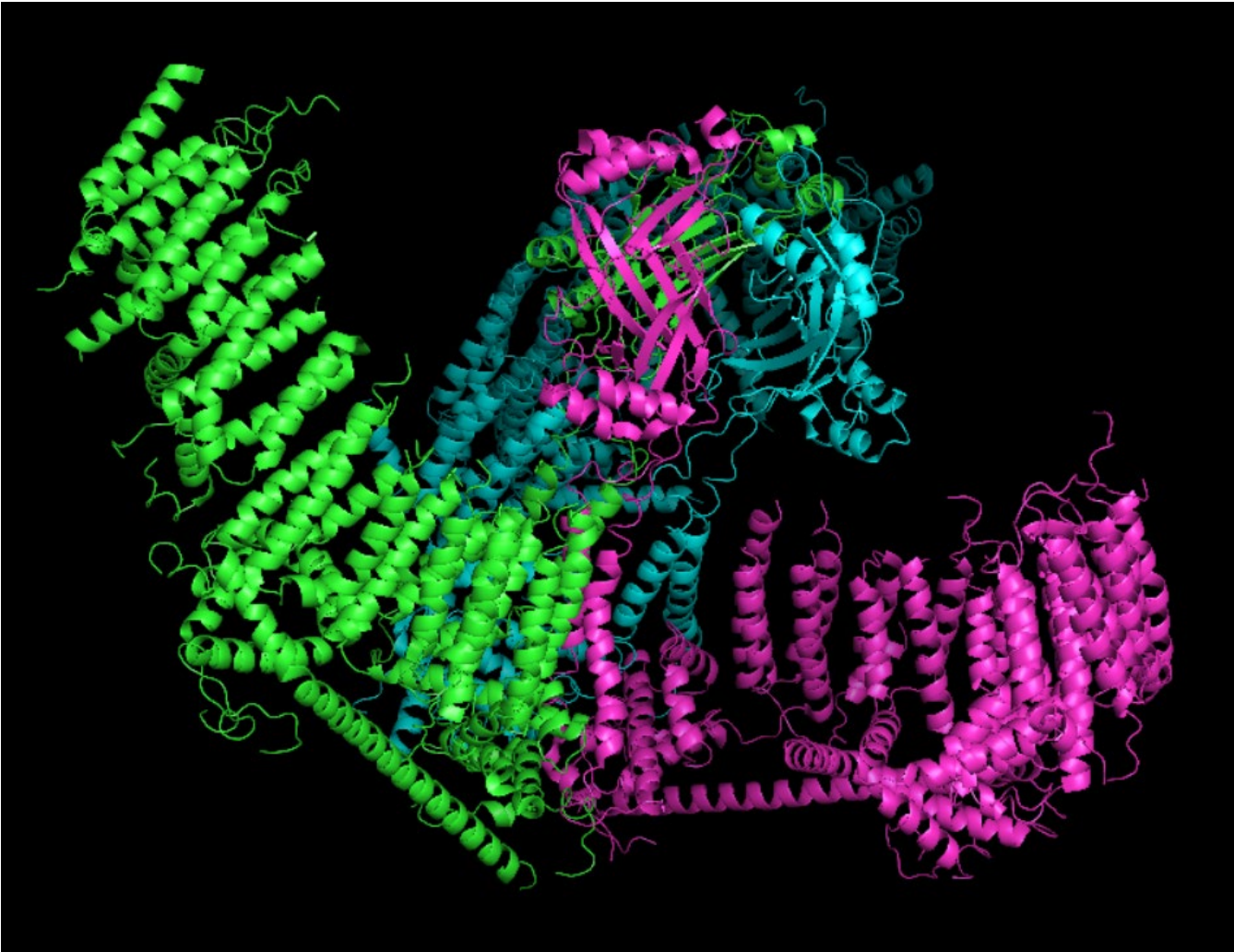


# Mutational sensitivity



# **Molecular docking of Yoda1 and Piezo1**

# Structure of Piezo1 and Yoda1



## Protocol

### 1. Process protein and ligand:

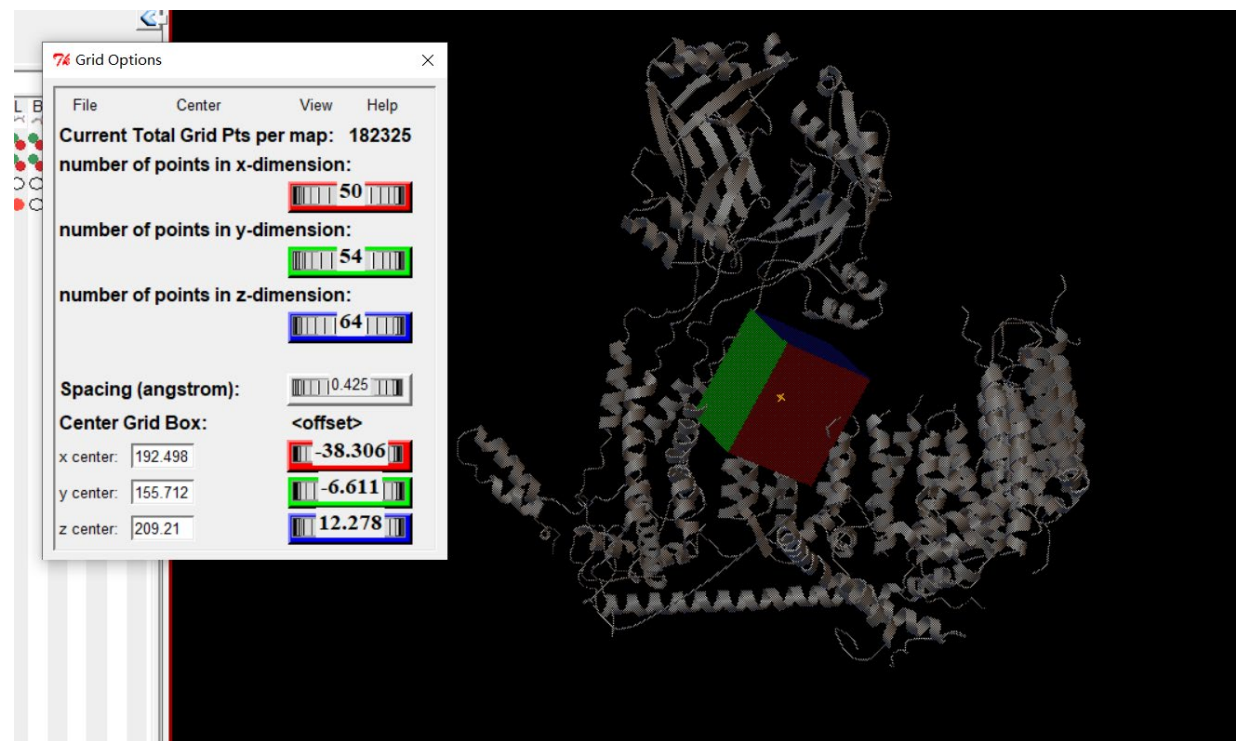
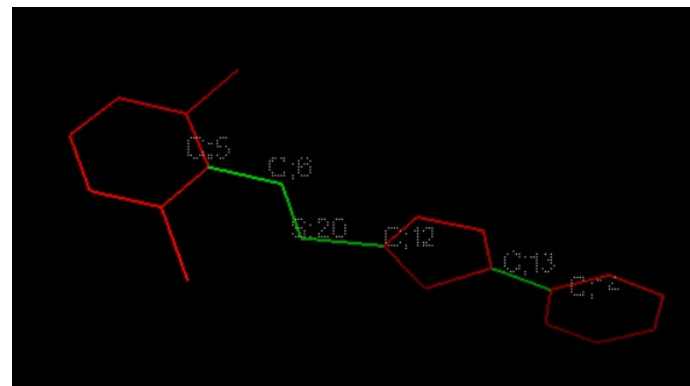
Add hydrogen and charges

### 2. Grid protein and ligand

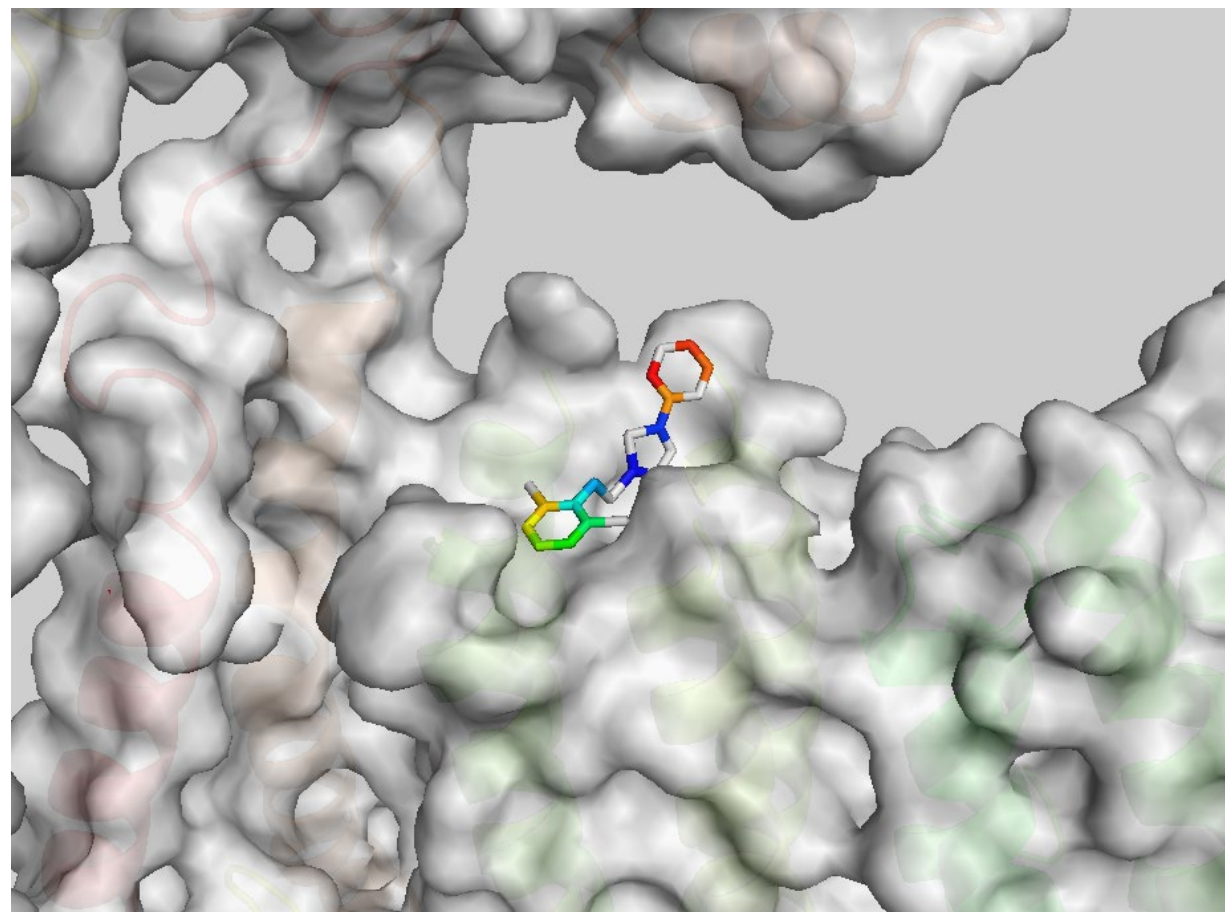
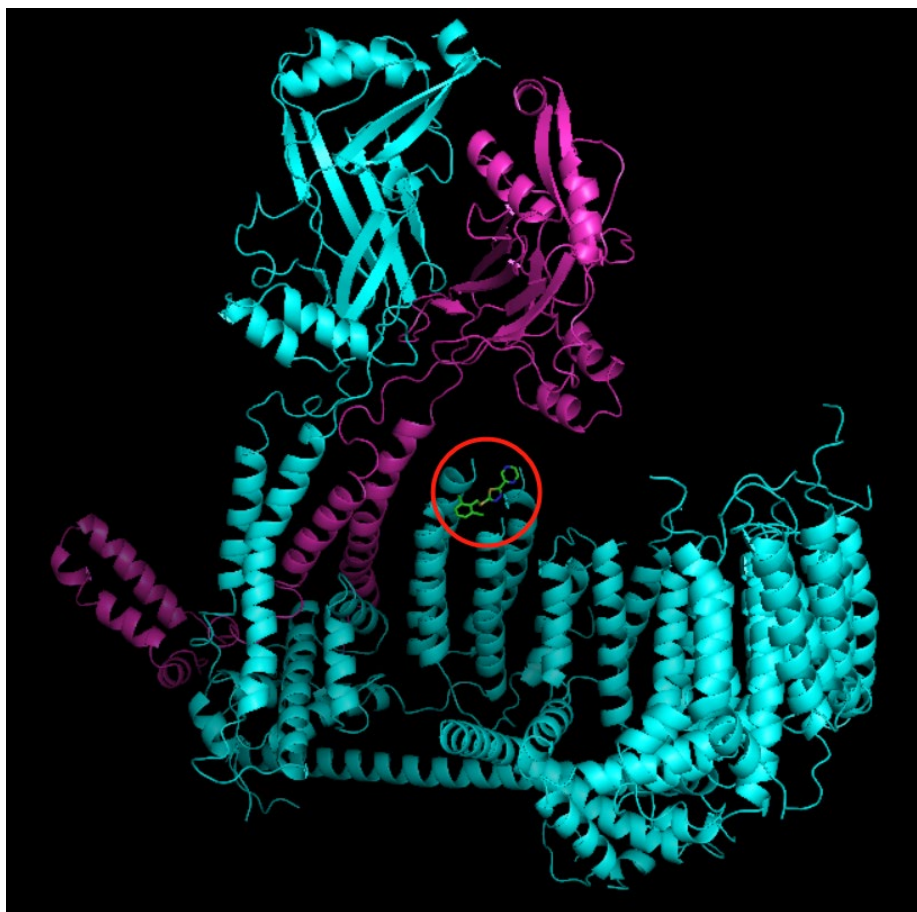
### 3. Dock ligand into grid box:

Genetic algorithm

### 4. Visualization



# Result



# Reference

- Wang, L., Zhou, H., Zhang, M. *et al.* (2019). Structure and mechanogating of the mammalian tactile channel PIEZO2. *Nature* **573**, 225–229
- Wu, J., Lewis, A. H., & Grandl, J. (2017). Touch, Tension, and Transduction - The Function and Regulation of Piezo Ion Channels. *Trends in biochemical sciences*, *42*(1), 57–71.
- Wu, J., Lewis, A.H., and Grandl, J. (2017a). Touch, Tension, and Transduction - The Function and Regulation of Piezo Ion Channels. *Trends Biochem Sci* *42*, 57-71.
- Coste, B., Mathur, J. *et al.* (2010). Piezo1 and Piezo2 Are Essential Components of Distinct Mechanically Activated Cation Channels. *Science* *330*, 55-60.
- Lumpkin, E.A., Marshall, K.L., and Nelson, A.M. (2010). The cell biology of touch. *J Cell Biol* *191*, 237-248.
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- Kefauver, J M *et al.* (2020). Discoveries in structure and physiology of mechanically activated ion channels. *Nature* vol.7835 : 567-576
- Wang, L., Zhou, H., *et al.* (2019). Structure and mechanogating of the mammalian tactile channel PIEZO2. *Nature*, *573*(7773), 225–229.
- Lacroix, J. J., *et al.* (2018). Probing the gating mechanism of the mechanosensitive channel Piezo1 with the small molecule Yoda1. *Nature communications*, *9*(1), 2029.



**Thanks for your attention!**