

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

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

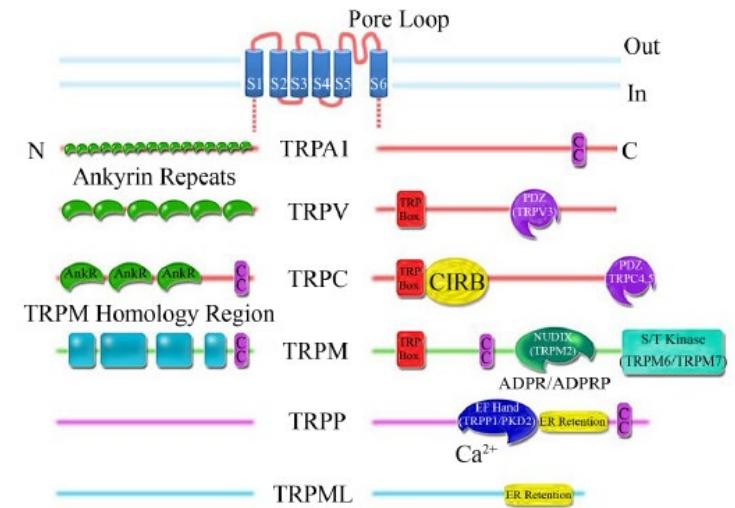
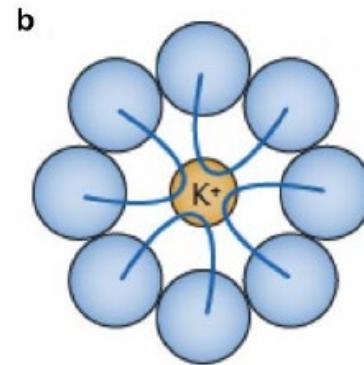
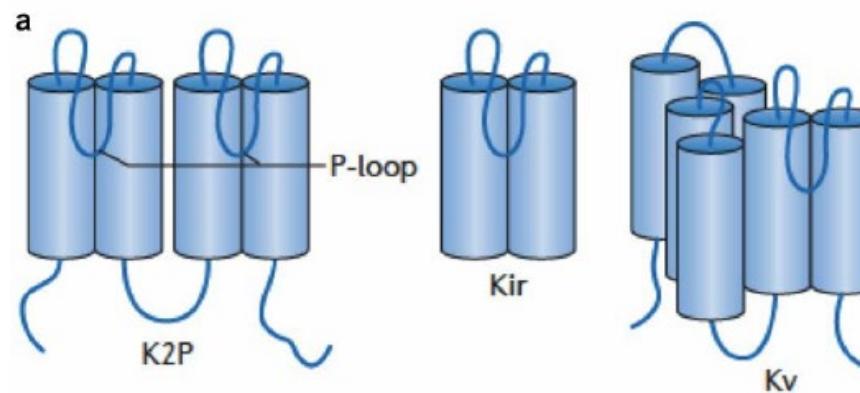
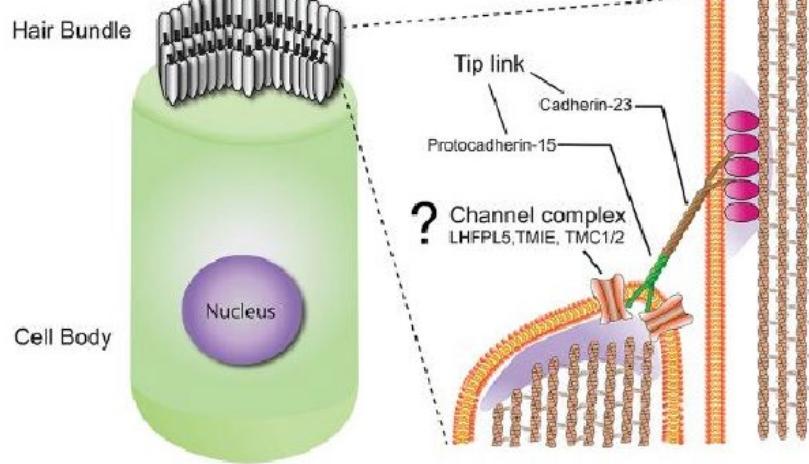
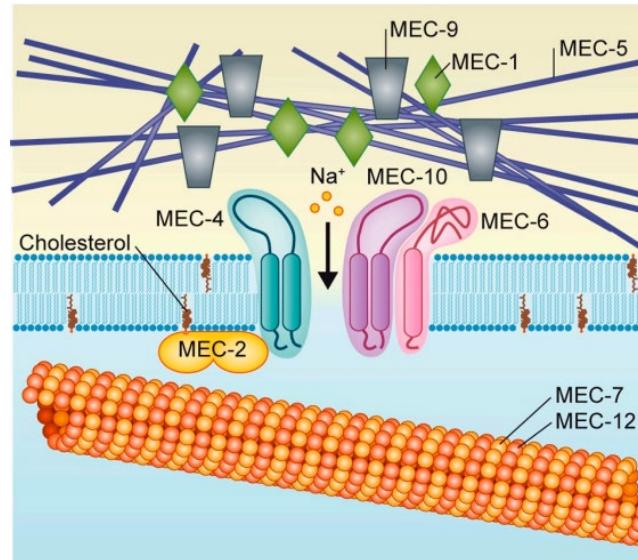
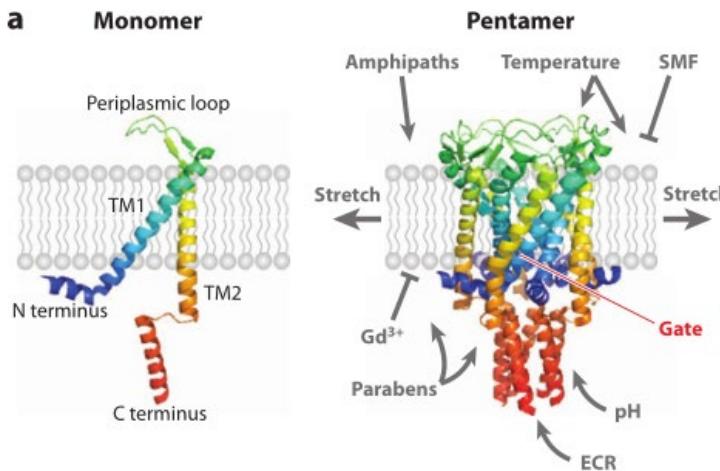
CONTENT

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

Mechanical feelings are closely related to life activities

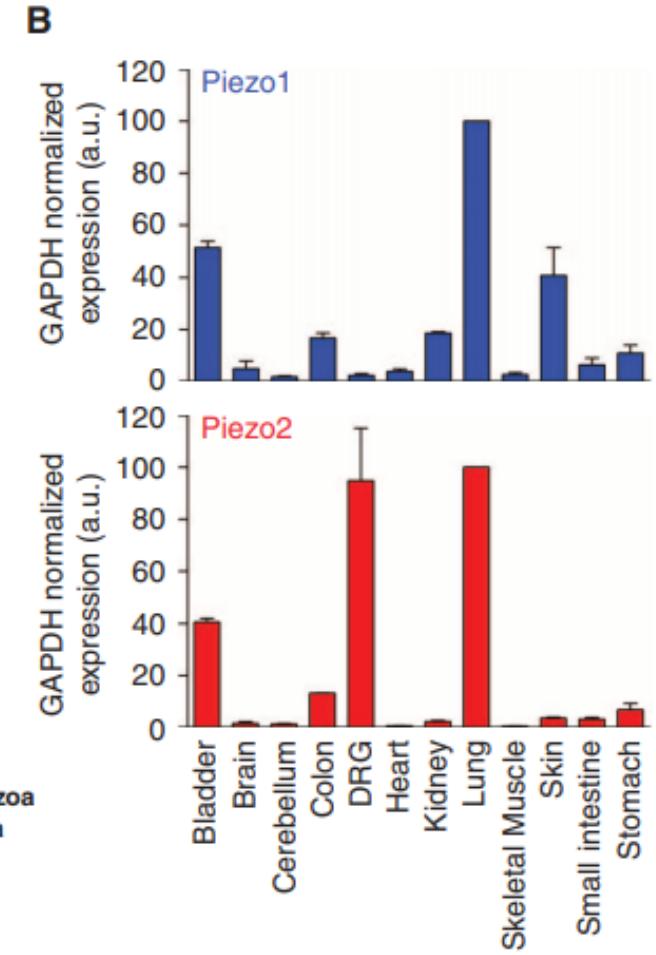
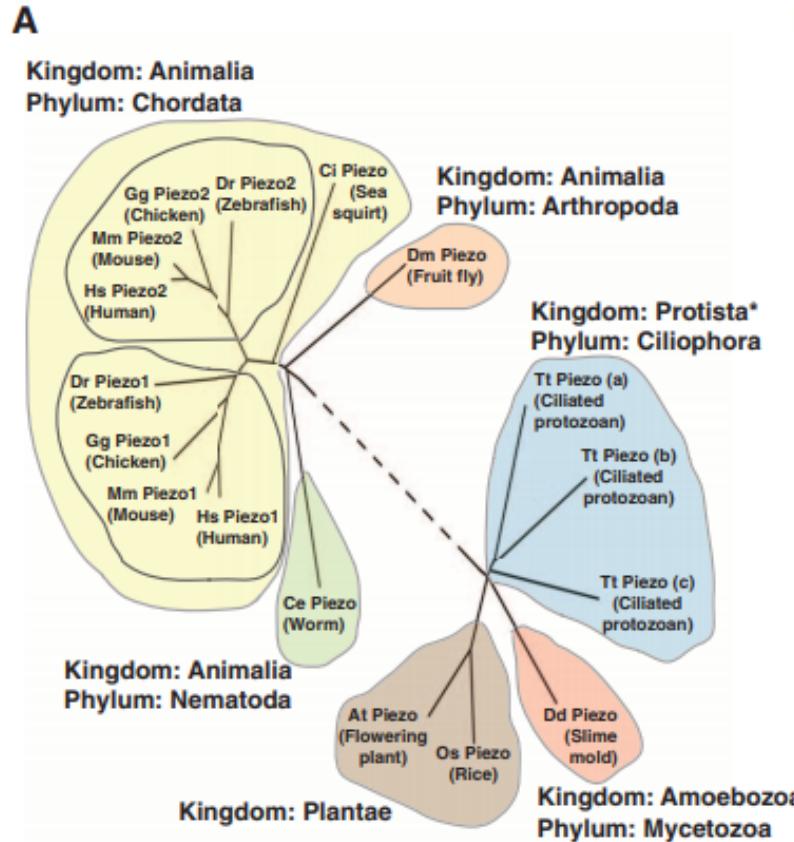
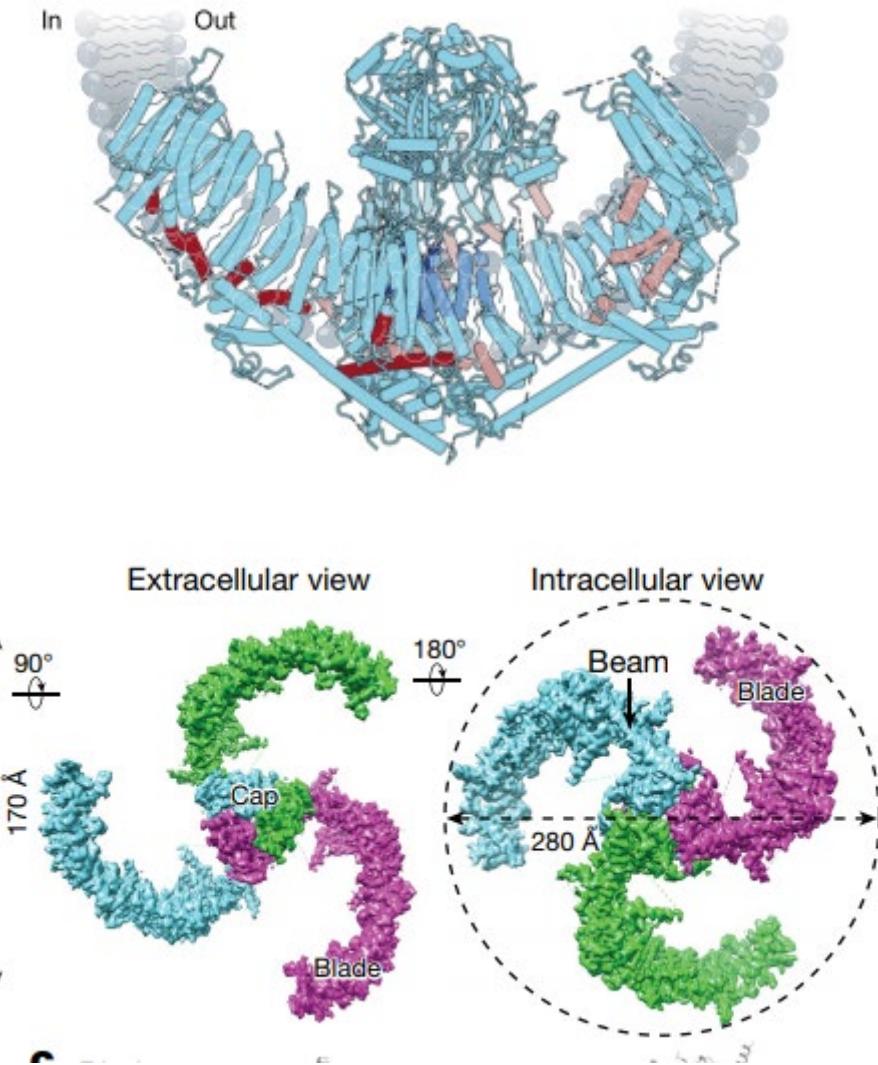


Mechanosensory related molecules in different organisms



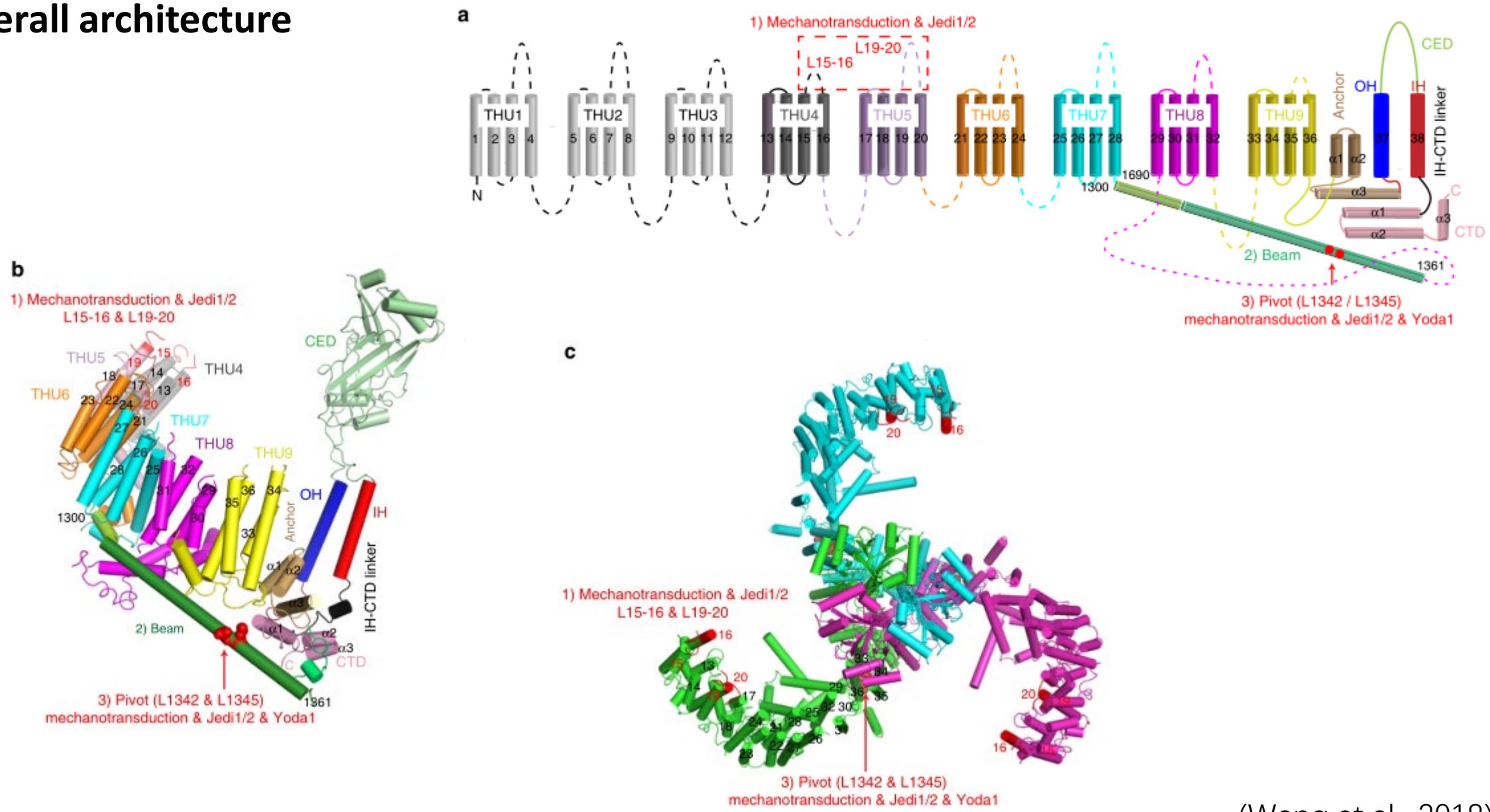
(Kung et al., 2010; Lumpkin et al., 2010)

The first identified class of cationic mechanotransducers in mammals



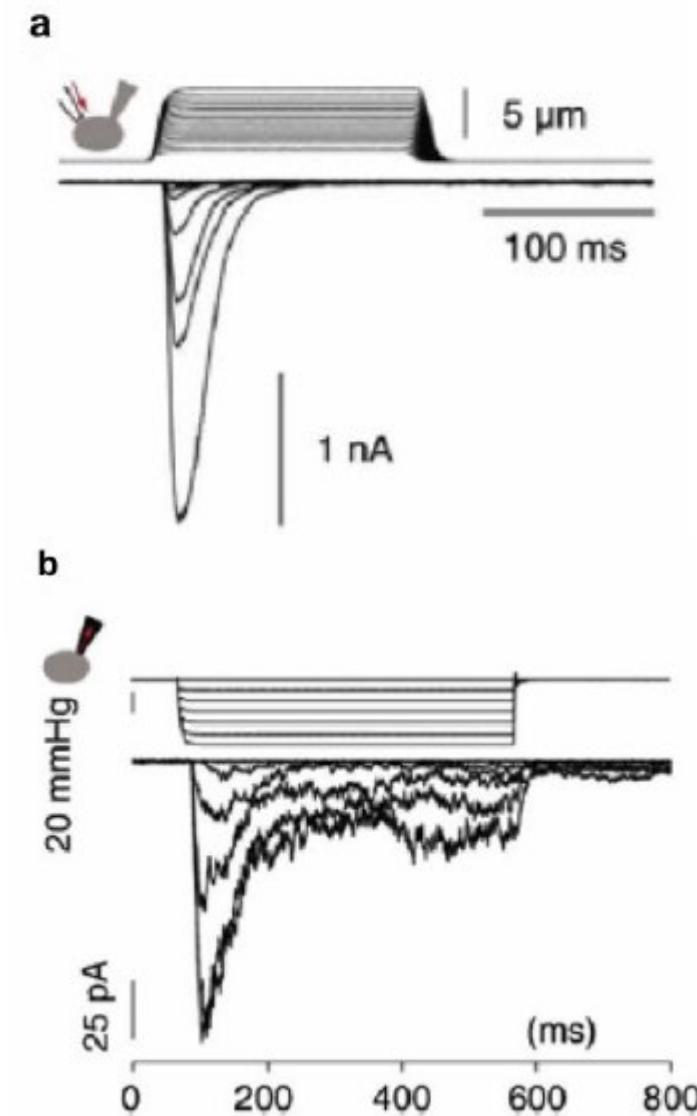
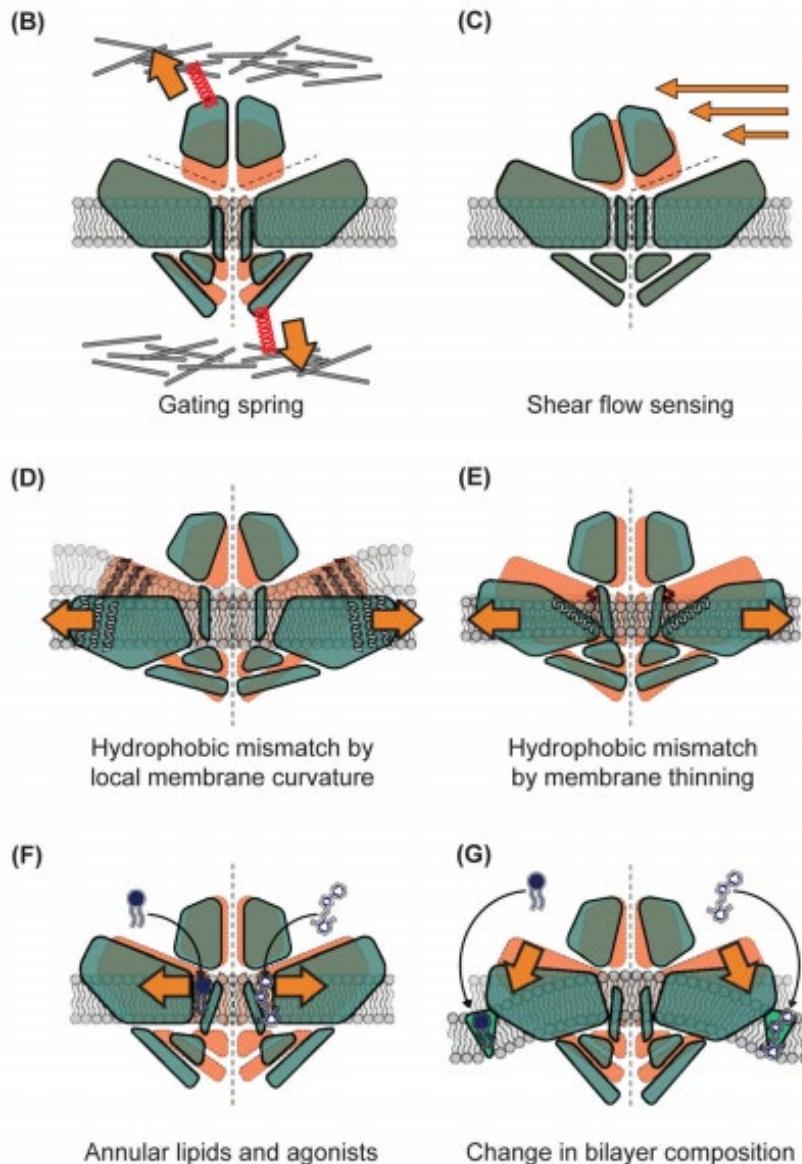
(Wang et al., 2019; Kefauver et al., 2020; Coste et al., 2010)

Overall architecture



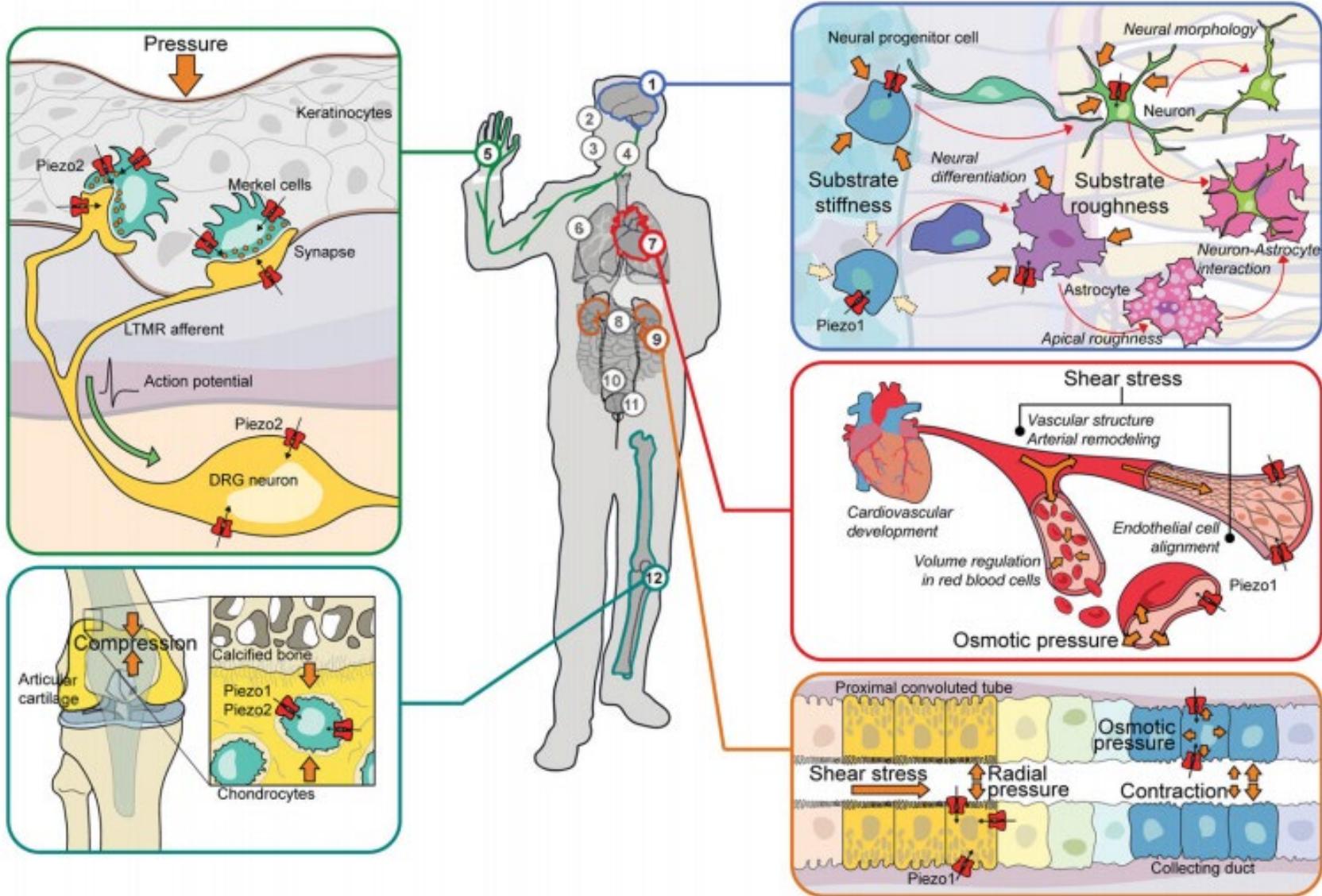
(Wang et al., 2018)

Gating mechanism and electrophysiological properties



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

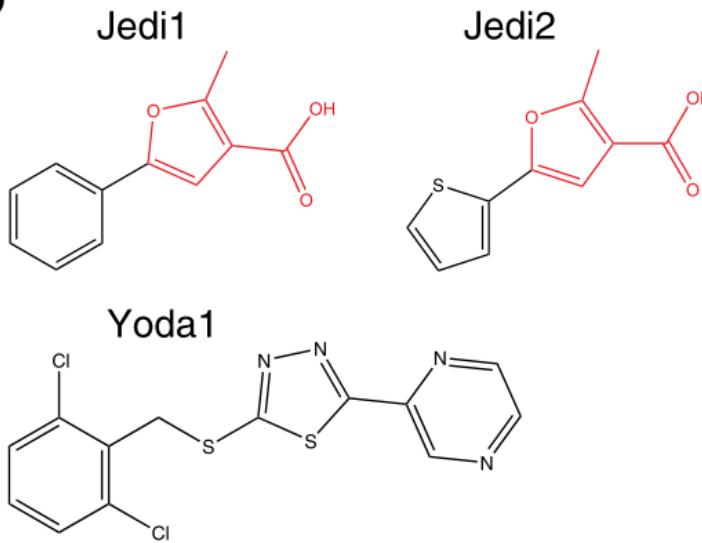
Expression and physiological roles of Piezos



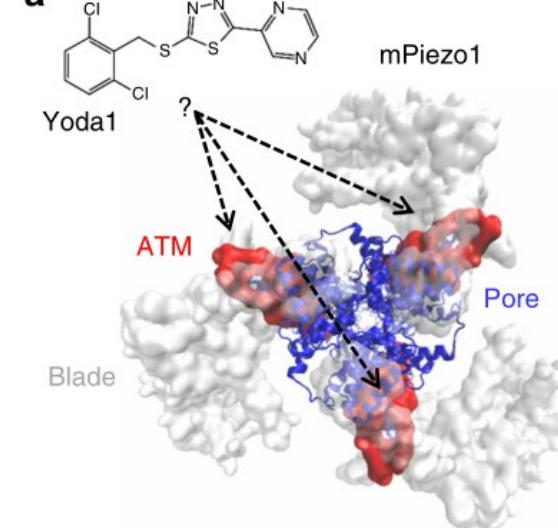
(Wu et al., 2017)

Lacking of pharmacological tools and unclear mechanisms hamper researches of Piezo1

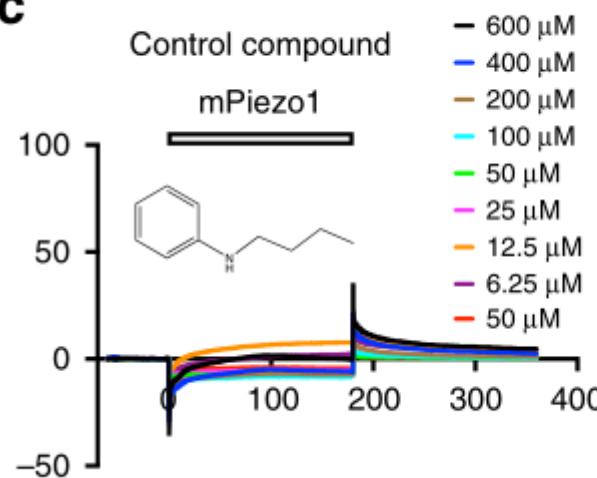
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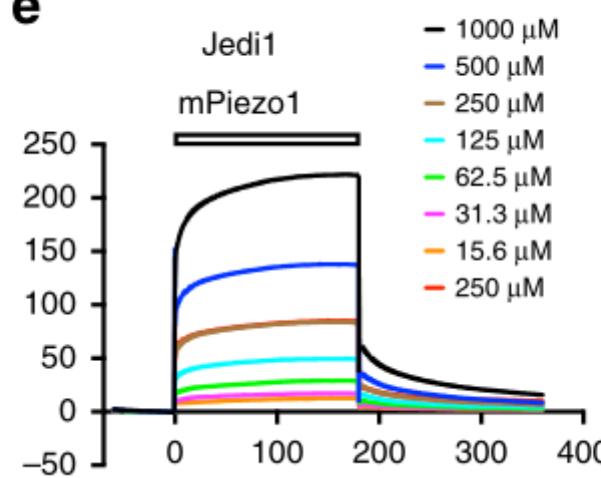
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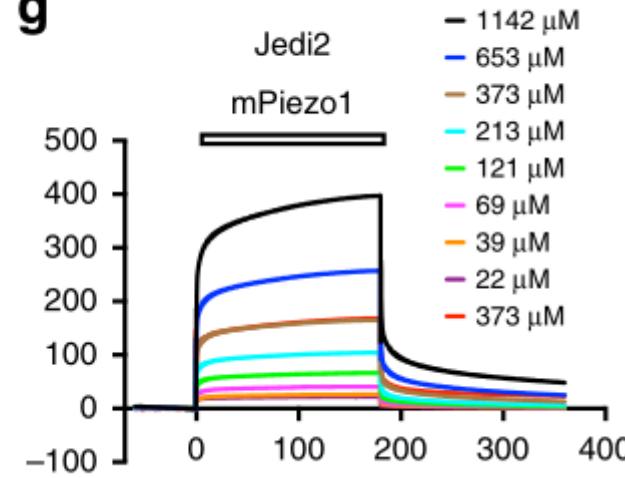
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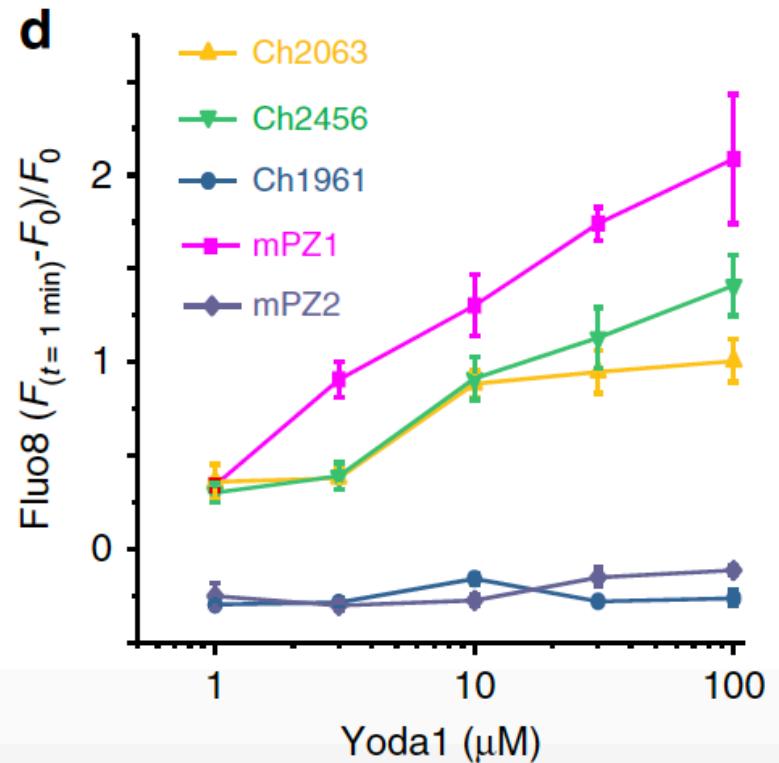
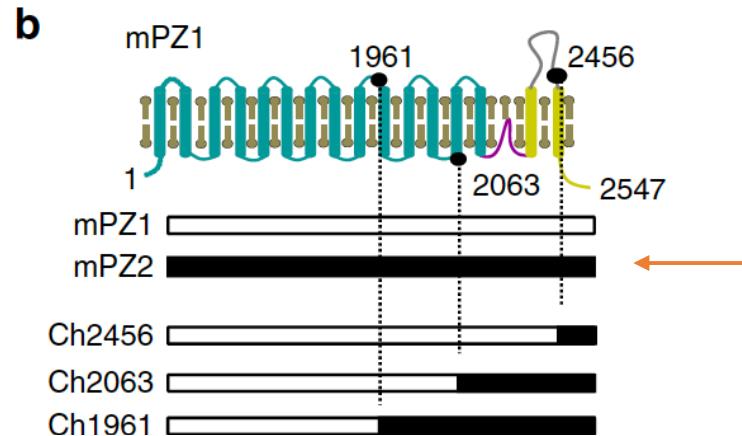
g



Research purposes

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

Needle Piezo family in Mouse for alignment



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

```

Piezol1 (*Mus musculus*) blast in Refseq_protein (in primates)

Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc Len	Accession
piezo-type mechanosensitive ion channel component 1 isoform X5 (<i>Rhinopithecus roxellana</i>)	<i>Rhinopithecus roxellana</i>	3949	3949	100%	0.0	81.52%	252	XP_030780187.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Trachypithecus francoisi</i>)	<i>Trachypithecus francoisi</i>	3949	3949	100%	0.0	81.34%	252	XP_03075225
PREDICTED: piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Macaca fasciata</i>)	<i>Macaca fasciularis</i>	3949	3949	100%	0.0	81.35%	252	XP_005592833.
piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Rhinopithecus roxellana</i>)	<i>Rhinopithecus roxellana</i>	3947	3947	100%	0.0	81.05%	254	XP_030780185.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Chlorocebus sabaeus</i>)	<i>Chlorocebus sabaeus</i>	3944	3944	100%	0.0	81.62%	252	XP_007792534.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Piliocolobus leprosicaeus</i>)	<i>Piliocolobus leprosicaeus</i>	3940	3940	100%	0.0	81.38%	252	XP_026303151.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Rhinopithecus roxellana</i>)	<i>Rhinopithecus roxellana</i>	3940	3940	99%	0.0	81.41%	254	XP_030780184.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Macaca mulatta</i>)	<i>Macaca mulatta</i>	3939	3939	100%	0.0	81.20%	252	XP_028693632.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Macaca nemestrina</i>)	<i>Macaca nemestrina</i>	3939	3939	100%	0.0	81.09%	252	XP_011751602.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Rhinopithecus roxellana</i>)	<i>Rhinopithecus roxellana</i>	3936	3936	99%	0.0	80.94%	256	XP_030780183.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Macaca nemestrina</i>)	<i>Macaca nemestrina</i>	3936	3936	100%	0.0	80.63%	254	XP_011751600.
PREDICTED: piezo-type mechanosensitive ion channel component 1 isoform X5 (<i>Cercopithecus</i>)	<i>Cercopithecus atys</i>	3933	3933	100%	0.0	81.47%	252	XP_011923129.
PREDICTED: piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Macaca fasciata</i>)	<i>Macaca fasciularis</i>	3930	3930	100%	0.0	79.73%	257	XP_015284294.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Hyllobates moloch</i>)	<i>Hyllobates moloch</i>	3929	3929	100%	0.0	80.71%	252	XP_032020985.
PREDICTED: piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Cercopithecus</i>)	<i>Cercopithecus atys</i>	3925	3925	100%	0.0	81.30%	254	XP_011922976.
PREDICTED: piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Cercopithecus</i>)	<i>Cercopithecus atys</i>	3923	3923	100%	0.0	80.92%	254	XP_011922885.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Otolemur garnettii</i>)	<i>Otolemur garnettii</i>	3920	3920	100%	0.0	80.26%	252	XP_026675111.
PREDICTED: piezo-type mechanosensitive ion channel component 1 (<i>Mandrillus leucophaeus</i>)	<i>Mandrillus leucophaeus</i>	3917	3917	99%	0.0	80.62%	256	XP_011878511.
PREDICTED: piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Cercopithecus</i>)	<i>Cercopithecus atys</i>	3916	3916	100%	0.0	80.76%	251	XP_011922804.
piezo-type mechanosensitive ion channel component 1 isoform X5 (<i>Calithrix jacchus</i>)	<i>Calithrix jacchus</i>	3904	3904	100%	0.0	80.77%	251	XP_03137966.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Pongo abelii</i>)	<i>Pongo abelii</i>	3900	3900	100%	0.0	80.66%	251	XP_024097831.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Pan troglodytes</i>)	<i>Pan troglodytes</i>	3898	3898	100%	0.0	80.51%	251	XP_016758686.
piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Pan paniscus</i>)	<i>Pan paniscus</i>	3898	3898	100%	0.0	80.28%	252	XP_034796799.
piezo-type mechanosensitive ion channel component 1 isoform X4 (<i>Calithrix jacchus</i>)	<i>Calithrix jacchus</i>	3894	3894	100%	0.0	80.09%	253	XP_03137965.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Pongo abelii</i>)	<i>Pongo abelii</i>	3894	3894	100%	0.0	80.54%	250	XP_024097832.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Calithrix jacchus</i>)	<i>Calithrix jacchus</i>	3890	3890	100%	0.0	79.99%	2542	XP_03137962.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Trachypithecus francoisi</i>)	<i>Trachypithecus francoisi</i>	3888	3888	100%	0.0	80.40%	259	XP_03075222.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Pan paniscus</i>)	<i>Pan paniscus</i>	3879	3879	99%	0.0	80.15%	258	XP_034796780.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Calithrix jacchus</i>)	<i>Calithrix jacchus</i>	3876	3876	100%	0.0	79.32%	256	XP_03137961.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Chlorocebus sabaeus</i>)	<i>Chlorocebus sabaeus</i>	3875	3875	100%	0.0	80.68%	250	XP_037864077.
piezo-type mechanosensitive ion channel component 1 isoform X8 (<i>Cebus imitator</i>)	<i>Cebus imitator</i>	3874	3874	100%	0.0	80.27%	251	XP_017368939.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Macaca mulatta</i>)	<i>Macaca mulatta</i>	3873	3873	100%	0.0	80.26%	250	XP_028693633.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Piliocolobus leprosicaeus</i>)	<i>Piliocolobus leprosicaeus</i>	3873	3873	100%	0.0	80.48%	250	XP_026303152.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Rhinopithecus roxellana</i>)	<i>Rhinopithecus roxellana</i>	3868	3868	99%	0.0	80.00%	2540	XP_030780186.
piezo-type mechanosensitive ion channel component 1 isoform X6 (<i>Calithrix jacchus</i>)	<i>Calithrix jacchus</i>	3867	3867	99%	0.0	79.21%	2560	XP_03137967.
piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Macaca nemestrina</i>)	<i>Macaca nemestrina</i>	3865	3865	100%	0.0	79.70%	252	XP_011751601.
piezo-type mechanosensitive ion channel component 1 isoform X7 (<i>Cebus imitator</i>)	<i>Cebus imitator</i>	3863	3863	100%	0.0	79.54%	253	XP_017368938.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Hyllobates moloch</i>)	<i>Hyllobates moloch</i>	3861	3861	100%	0.0	79.81%	2510	XP_032020199.
PREDICTED: piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Macaca fasciata</i>)	<i>Macaca fasciularis</i>	3856	3856	100%	0.0	78.81%	254	XP_015284245.
piezo-type mechanosensitive ion channel component 1 isoform X8 (<i>Cebus imitator</i>)	<i>Cebus imitator</i>	3851	3851	100%	0.0	78.78%	256	XP_037591919.
PREDICTED: piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Cercopithecus</i>)	<i>Cercopithecus atys</i>	3847	3847	100%	0.0	79.93%	252	XP_011923066.
piezo-type mechanosensitive ion channel component 1 isoform X8 (<i>Sapajus apella</i>)	<i>Sapajus apella</i>	3845	3845	100%	0.0	80.38%	2517	XP_021405699.
piezo-type mechanosensitive ion channel component 1 isoform X5 (<i>Cebus imitator</i>)	<i>Cebus imitator</i>	3843	3843	100%	0.0	78.42%	2576	XP_017369387.
piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Cebus imitator</i>)	<i>Cebus imitator</i>	3835	3835	100%	0.0	78.36%	2579	XP_037591911.
piezo-type mechanosensitive ion channel component 1 isoform X7 (<i>Sapajus apella</i>)	<i>Sapajus apella</i>	3834	3834	100%	0.0	79.65%	253	XP_02140566.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Pan troglodytes</i>)	<i>Pan troglodytes</i>	3830	3830	100%	0.0	79.57%	2492	XP_01678567.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Cebus imitator</i>)	<i>Cebus imitator</i>	3827	3827	100%	0.0	77.67%	2601	XP_037591919.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Cebus imitator</i>)	<i>Cebus imitator</i>	3826	3826	100%	0.0	77.11%	2601	XP_037591919.
piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Pongo abelii</i>)	<i>Pongo abelii</i>	3825	3825	100%	0.0	79.60%	2498	XP_02409740.
piezo-type mechanosensitive ion channel component 1 isoform X6 (<i>Sapajus apella</i>)	<i>Sapajus apella</i>	3817	3817	100%	0.0	78.89%	2564	XP_02140567.
piezo-type mechanosensitive ion channel component 1 isoform X5 (<i>Sapajus apella</i>)	<i>Sapajus apella</i>	3814	3814	100%	0.0	78.53%	2576	XP_02140566.
piezo-type mechanosensitive ion channel component 1 isoform X7 (<i>Sapajus apella</i>)	<i>Sapajus apella</i>	3810	3810	99%	0.0	79.21%	2568	XP_034796780.
piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Calithrix jacchus</i>)	<i>Calithrix jacchus</i>	3810	3810	100%	0.0	78.40%	2540	XP_03137963.
piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Sapajus apella</i>)	<i>Sapajus apella</i>	3803	3803	100%	0.0	78.48%	2579	XP_023140564.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Sapajus apella</i>)	<i>Sapajus apella</i>	3797	3797	100%	0.0	77.79%	2601	XP_03140562.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Sapajus apella</i>)	<i>Sapajus apella</i>	3796	3796	100%	0.0	77.82%	2600	XP_03140561.
piezo-type mechanosensitive ion channel component 1 isoform X4 (<i>Cebus imitator</i>)	<i>Cebus imitator</i>	3795	3795	100%	0.0	77.07%	2577	XP_037591912.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Microcebus murinus</i>)	<i>Microcebus murinus</i>	3793	3793	100%	0.0	79.84%	2502	XP_012592580.
piezo-type mechanosensitive ion channel component 1 isoform X1 (<i>Papio anubis</i>)	<i>Papio anubis</i>	3778	3778	100%	0.0	78.99%	2541	XP_03154485.
piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Chlorocebus sabaeus</i>)	<i>Chlorocebus sabaeus</i>	3776	3776	93%	0.0	82.15%	2397	XP_007925355.
piezo-type mechanosensitive ion channel component 1 isoform X2 (<i>Microcebus murinus</i>)	<i>Microcebus murinus</i>	3766	3766	100%	0.0	78.98%	2477	XP_021385569.
piezo-type mechanosensitive ion channel component 1 isoform X4 (<i>Sapajus apella</i>)	<i>Sapajus apella</i>	3760	3760	100%	0.0	76.95%	2577	XP_02140565.
piezo-type mechanosensitive ion channel component 1 (<i>Aotus naremicus</i>)	<i>Aotus naremicus</i>	3751	3751	92%	0.0	81.58%	234	XP_021526701.
PREDICTED: piezo-type mechanosensitive ion channel component 1 (<i>Propithecus coquereli</i>)	<i>Propithecus coquereli</i>	3657	3657	91%	0.0	82.06%	2281	XP_021512314.
PREDICTED: piezo-type mechanosensitive ion channel component 1 (<i>Colobus angolensis pallatus</i>)	<i>Colobus angolensis pallatus</i>	3645	3645	89%	0.0	82.49%	2281	XP_01734864.
piezo-type mechanosensitive ion channel component 1 isoform X3 (<i>Trachypithecus francoisi</i>)	<i>Trachypithecus francoisi</i>	3571	3571	87%	0.0	82.70%	2222	XP_03075223.
piezo-type mechanosensitive ion channel component 1 isoform X4 (<i>Macaca nemestrina</i>)	<i>Macaca nemestrina</i>	3559	3559	87%	0.0	81.98%	2233	XP_011751604.
PREDICTED: piezo-type mechanosensitive ion channel component 1 isoform X6 (<i>Cercopithecus</i>)	<i>Cercopithecus atys</i>	3542	3542	87%	0.0	82.16%	2244	XP_011923024.

Piezol1 (*Mus musculus*) blast in UniprotKB/Swiss-Prot

Descriptions Graphic Summary Alignments Taxonomy

Sequences producing significant alignments Download New Select columns Show 100

select all 7 sequences selected GenPept Graphics Distance tree of results Multiple alignment New 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...	Rattus norvegicus	4627	4627	100%	0.0	93.49%	2535	Q0KL00.3
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel component 1; AltName: Full=Membrane protein ind...	Homo sapiens	3896	3896	100%	0.0	80.19%	2521	Q92508.4
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel component 2; AltName: Full=Protein FAM38B.[Hom...]	Homo sapiens	1023	2197	97%	0.0	43.35%	2752	Q9H5I5.2
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel component [Drosophila melanogaster]	Drosophila mela...	459	1023	88%	7e-129	26.87%	2551	M9MSG8.1
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel component 1 [Caenorhabditis elegans]	Caenorhabditis...	451	750	95%	1e-126	31.20%	2442	AOA061ACU2.1
<input checked="" type="checkbox"/>	RecName: Full=Protein PIEZO homolog [Dictyostelium discoideum]	Dictyostelium dis...	222	269	29%	2e-56	25.55%	3080	Q54S52.1
<input checked="" type="checkbox"/>	RecName: Full=Piezo-type mechanosensitive ion channel homolog [Arabidopsis thaliana]	Arabidopsis thali...	196	239	26%	2e-48	27.30%	2462	F4IN58.1

Query seq. Specific hits Superfamilies

Distribution of the top 14 Blast Hits on 7 subject sequences

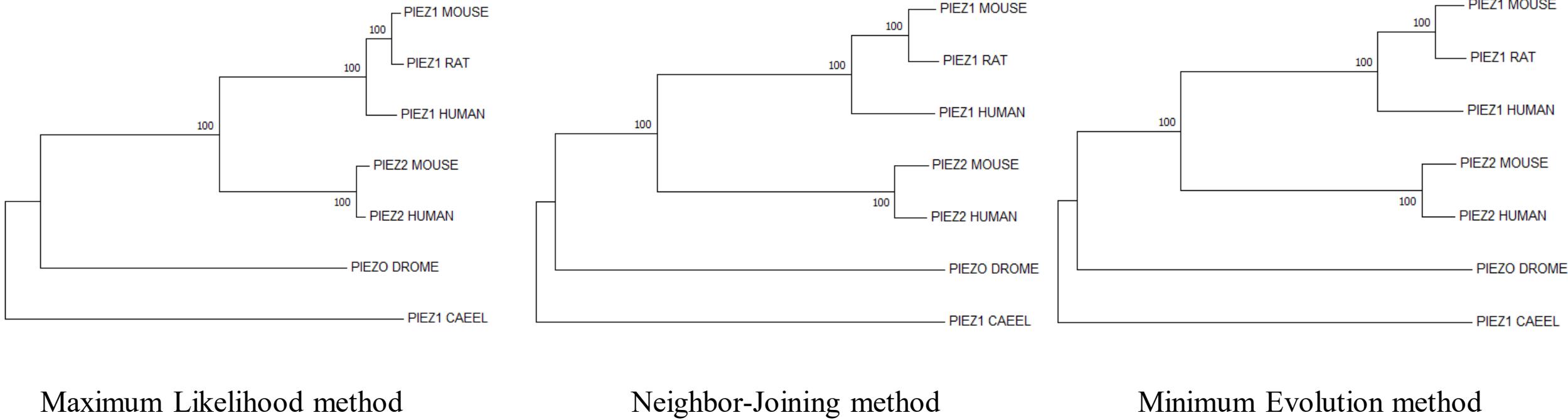
Query 1 500 1000 1500 2000 2500

Reviewed Piezo family in UniprotKB

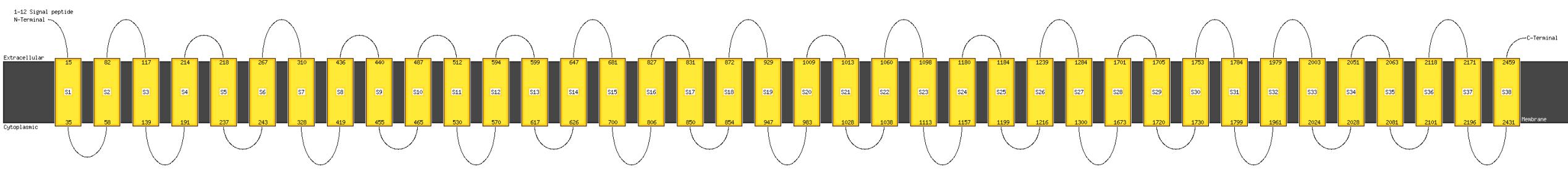
Entry	Entry name		Protein names	Gene names	Organism	Length
E2JF22	PIEZ1_MOUSE		Piezo-type mechanosensitive ion cha...	Piezo1 Fam38a	Mus musculus (Mouse)	2,547
Q9Z508	PIEZ1_HUMAN		Piezo-type mechanosensitive ion cha...	PIEZ01 FAM38A, KIAA0233	Homo sapiens (Human)	2,521
Q9H5I5	PIEZ2_HUMAN		Piezo-type mechanosensitive ion cha...	PIEZ02 C18orf30, C18orf58, FAM38B	Homo sapiens (Human)	2,752
Q8CD54	PIEZ2_MOUSE		Piezo-type mechanosensitive ion cha...	Piezo2 Fam38b	Mus musculus (Mouse)	2,822
Q0KL00	PIEZ1_RAT		Piezo-type mechanosensitive ion cha...	Piezo1 Fam38a	Rattus norvegicus (Rat)	2,535
A0A061ACU2	PIEZ1_CAEEL		Piezo-type mechanosensitive ion cha...	pezo-1 C10C5.1	Caenorhabditis elegans	2,442
M9MSG8	PIEZO_DROME		Piezo-type mechanosensitive ion cha...	Piezo CG18103	Drosophila melanogaster (Fruit fly)	2,551

Reviewed Piezo family in MEGA

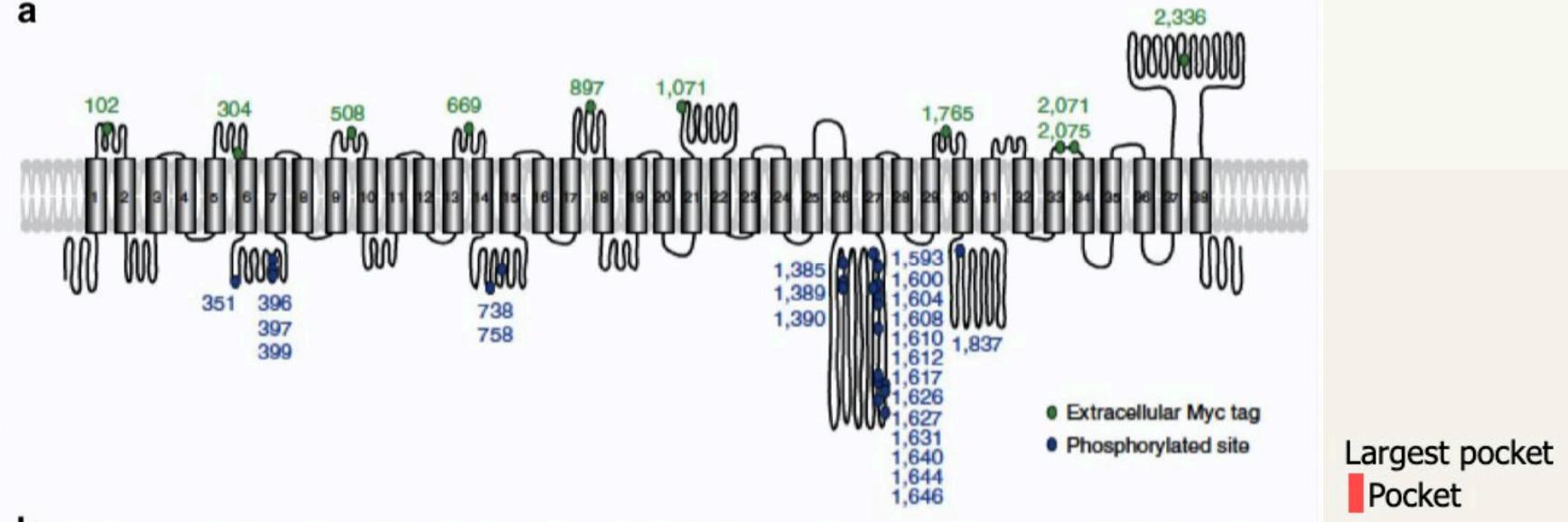
Reviewed Piezo family in MEGA



Piezol1 (*Homo sapien*) predicted on Phyre2 web

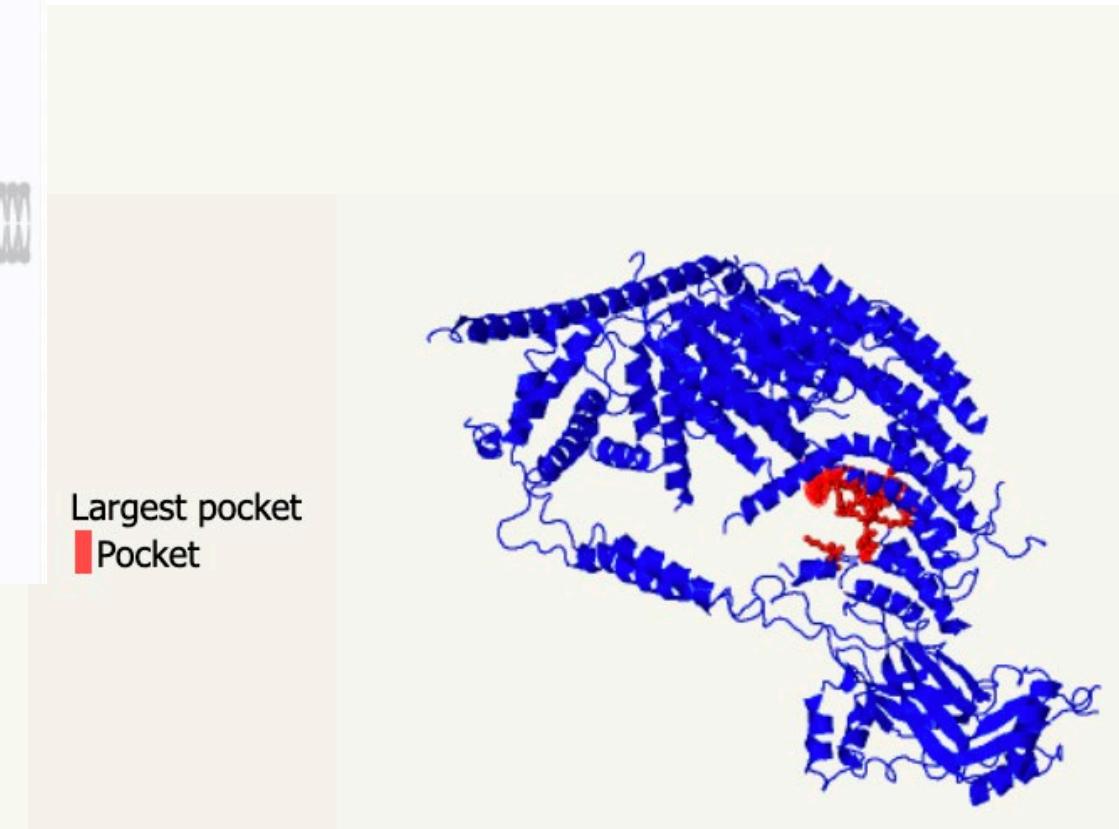


a

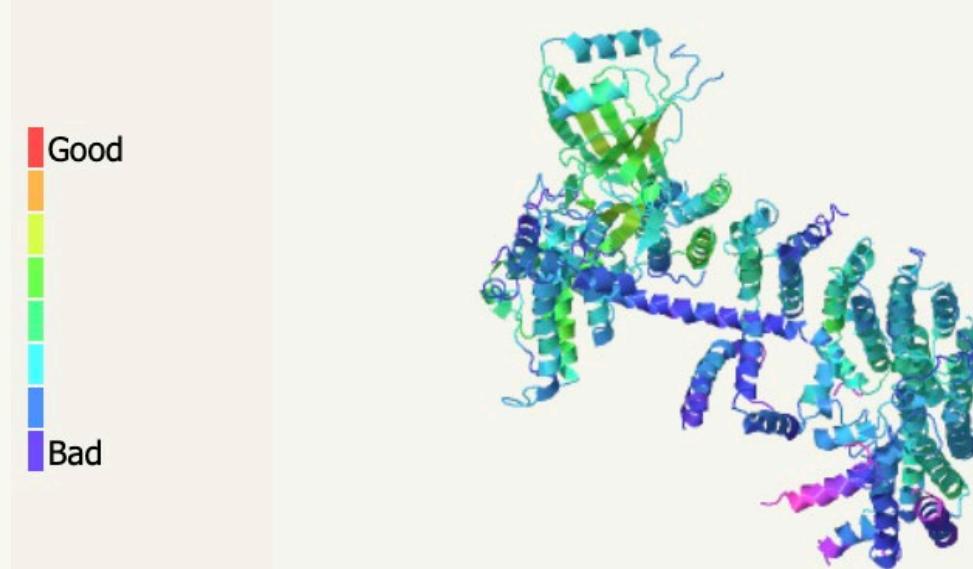
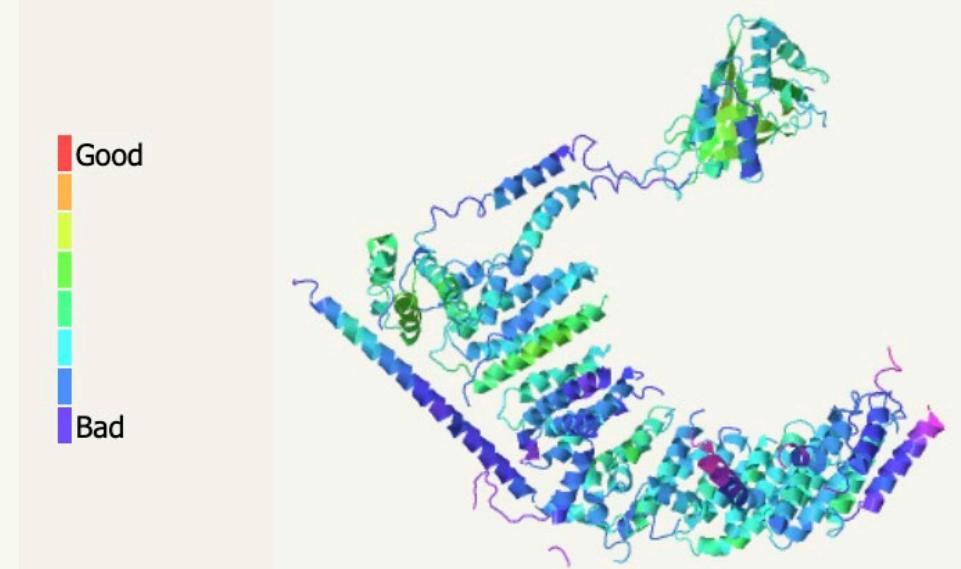


Piezol1_Mouse

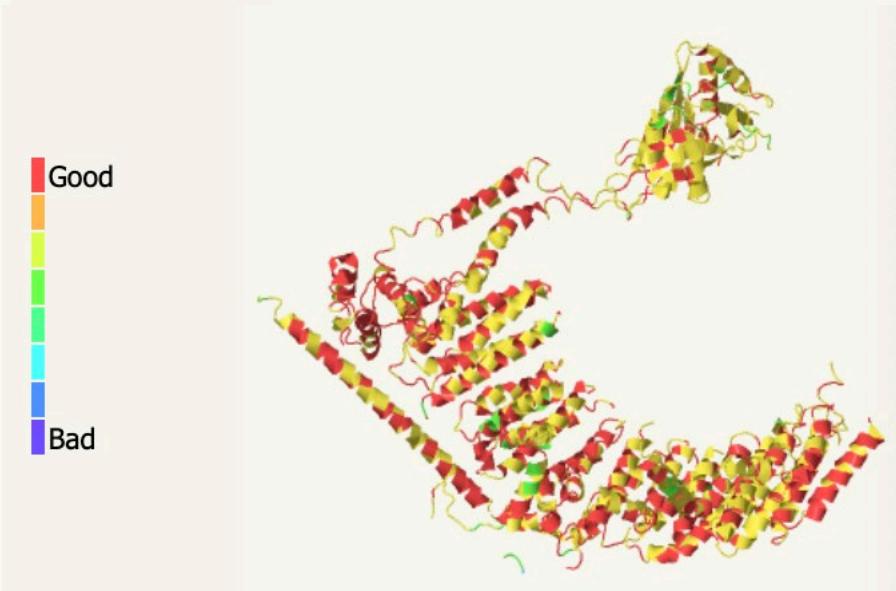
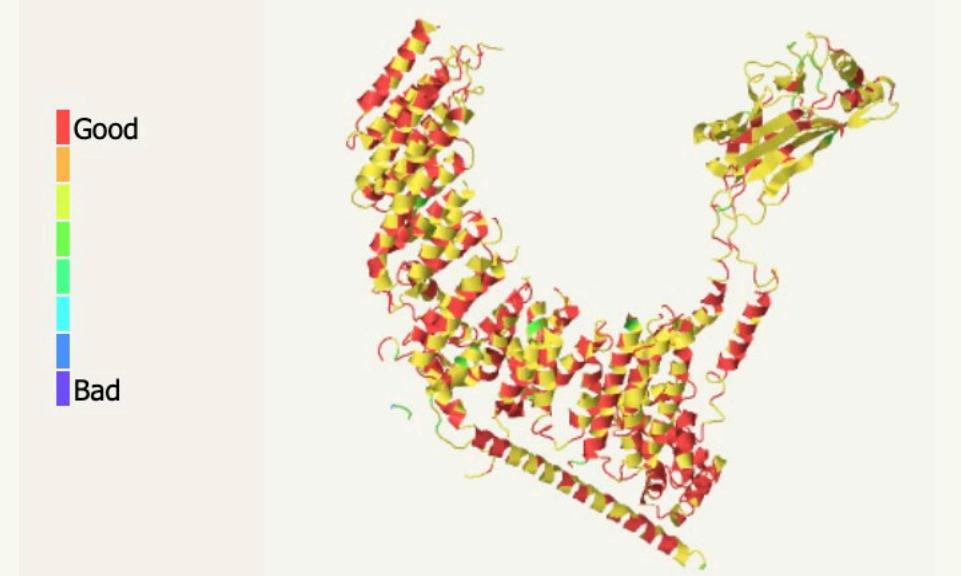
Coste et al., 2015



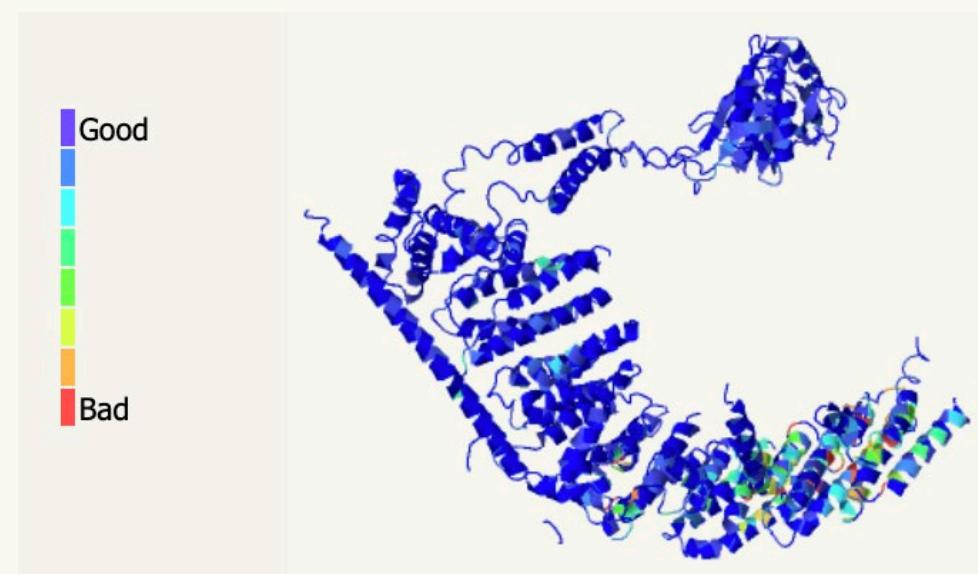
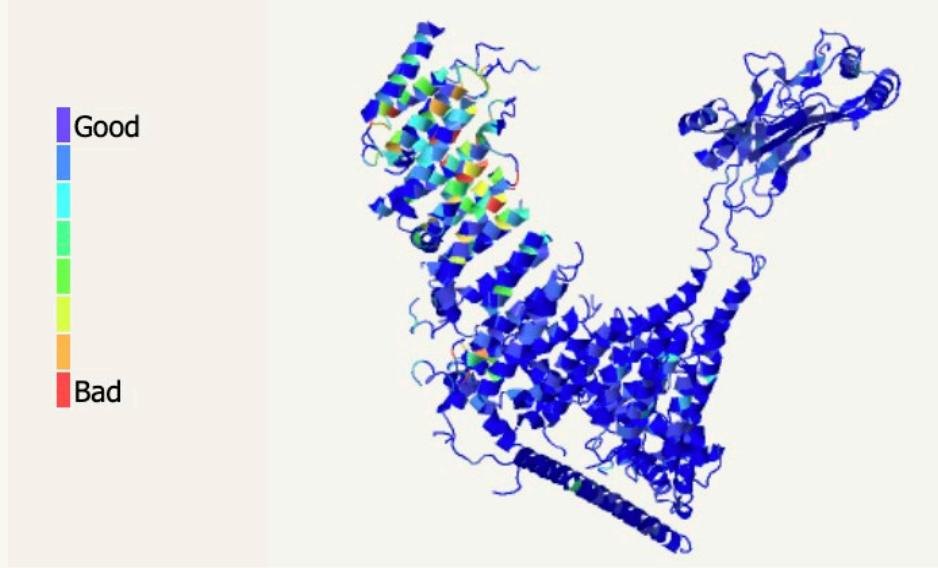
ProQ2 quality assessment



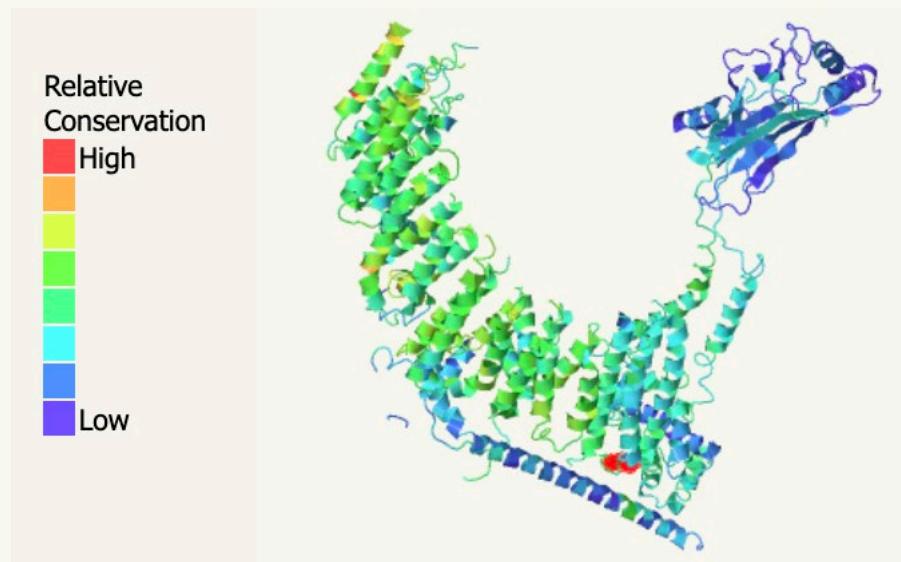
Alignment Confidence



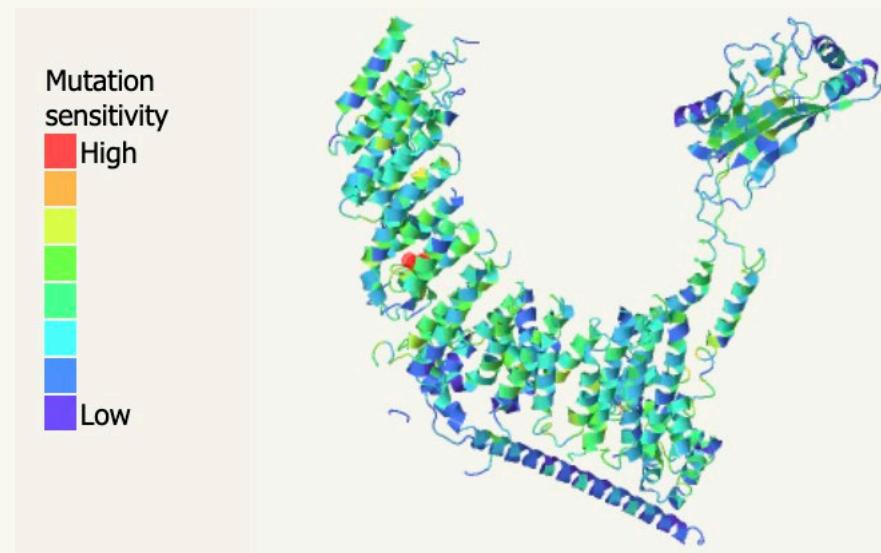
Clash Analysis



Conservation

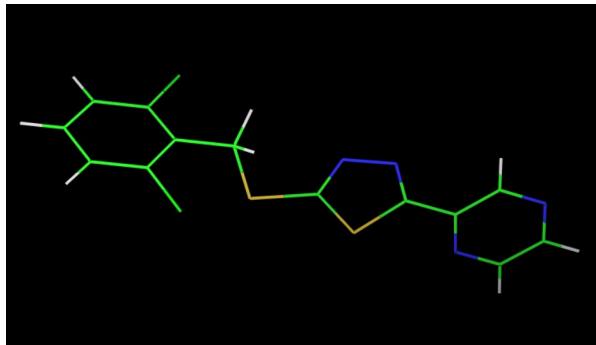
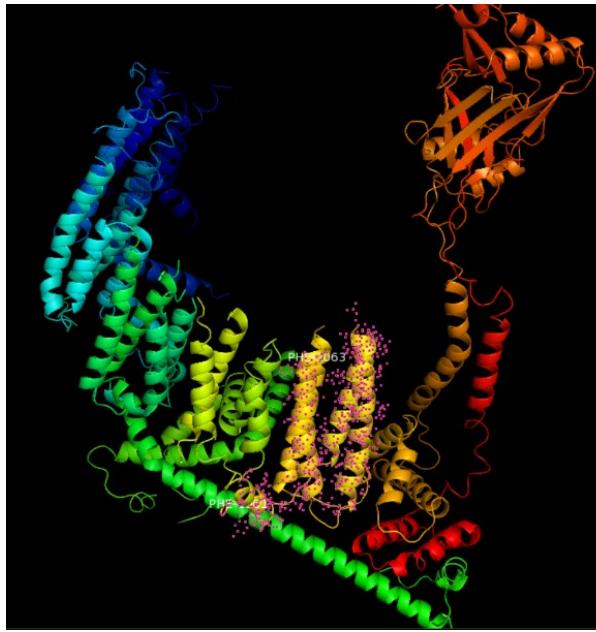
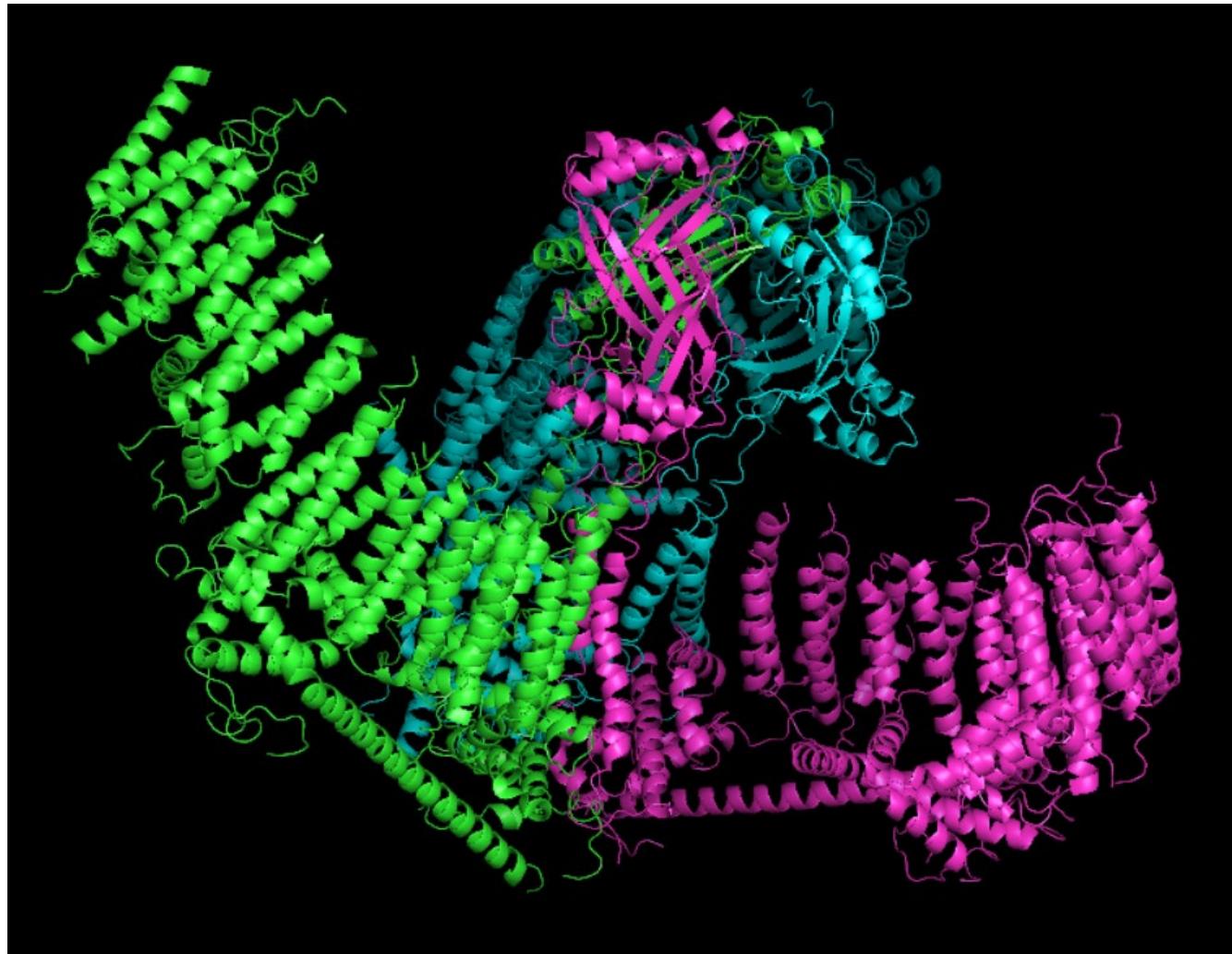


Mutational sensitivity



Molecular docking of Yoda1 and Piezo1

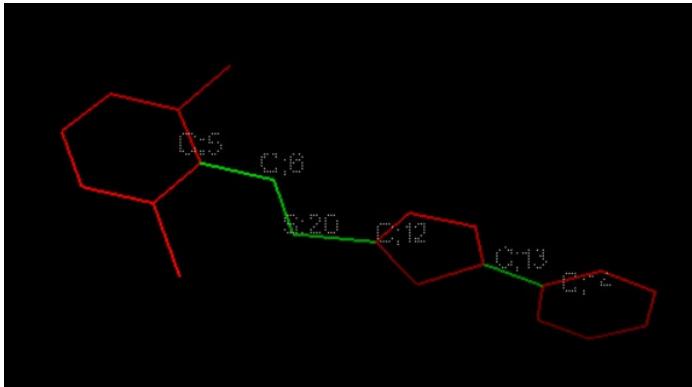
Structure of Piezo1 and Yoda1



Protocol

1. Process protein and ligand:

Add hydrogen and charges

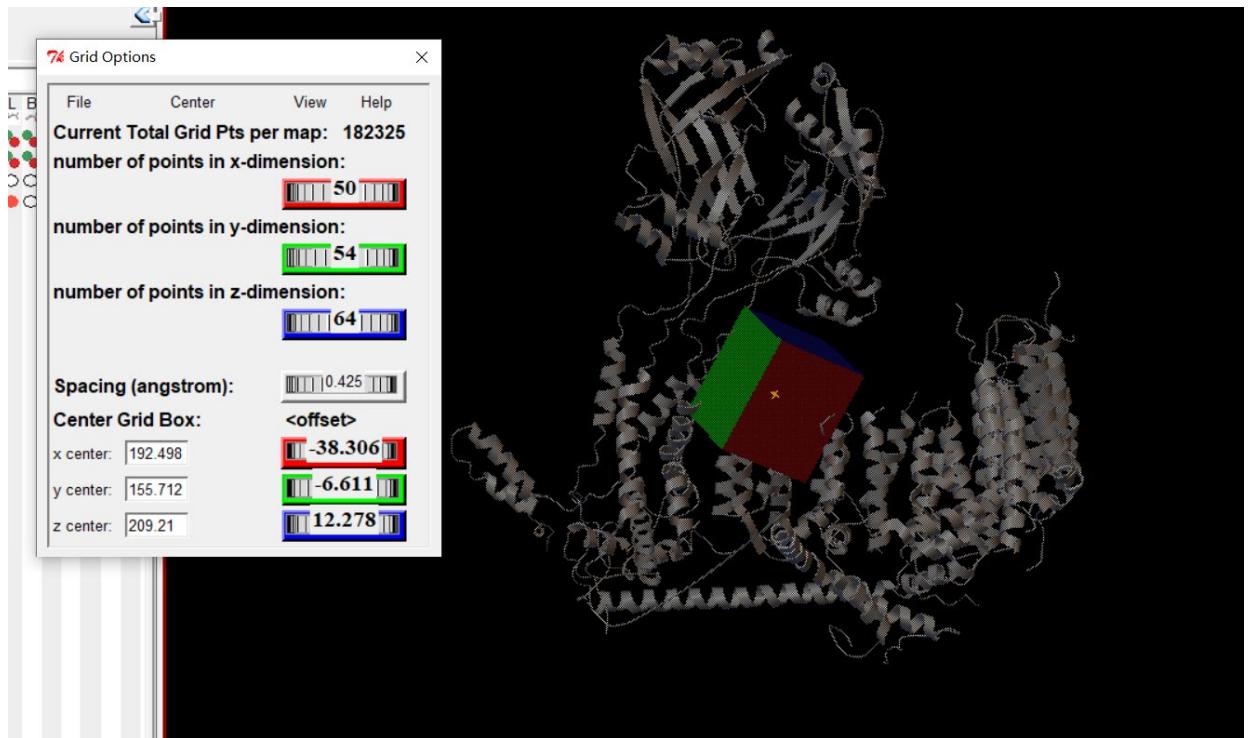


2. Grid protein and ligand

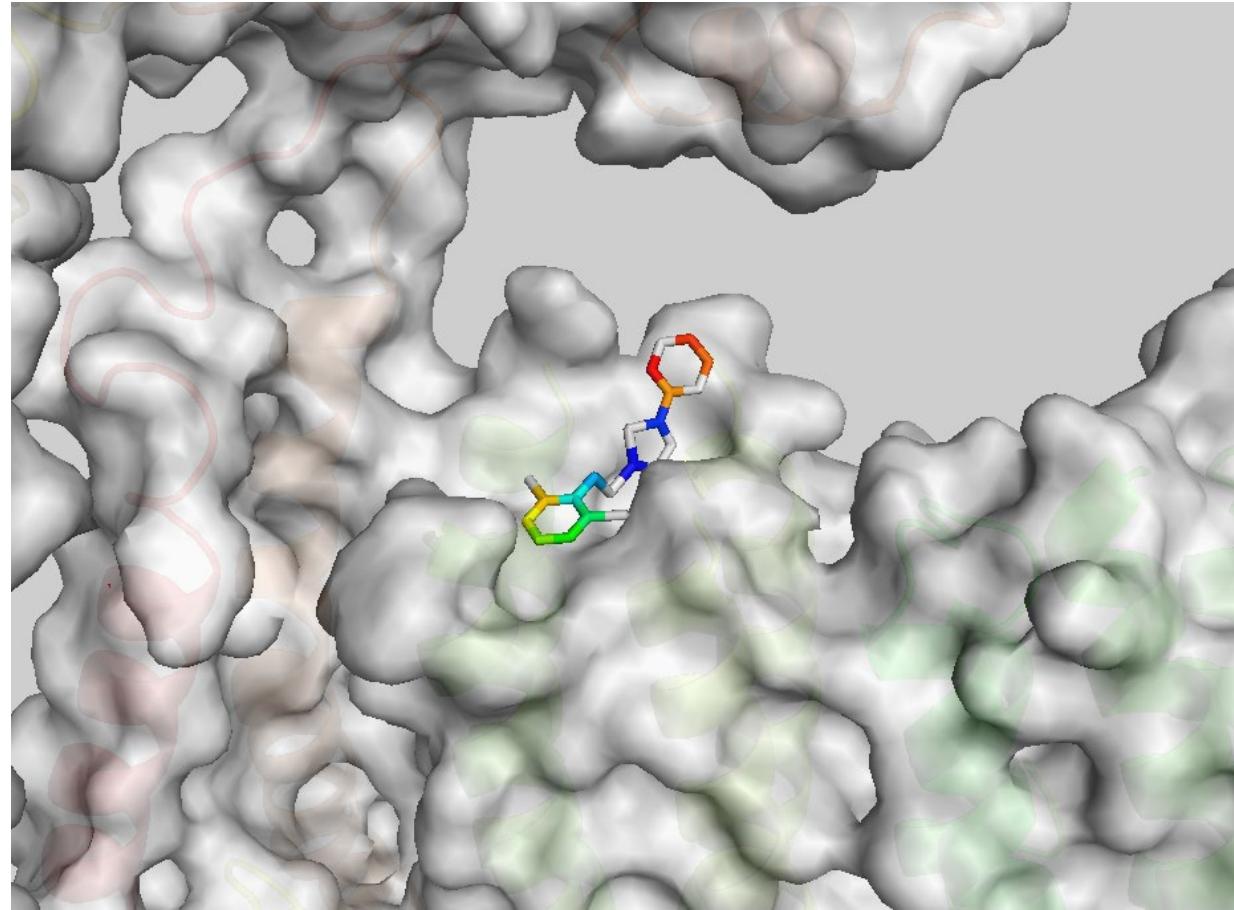
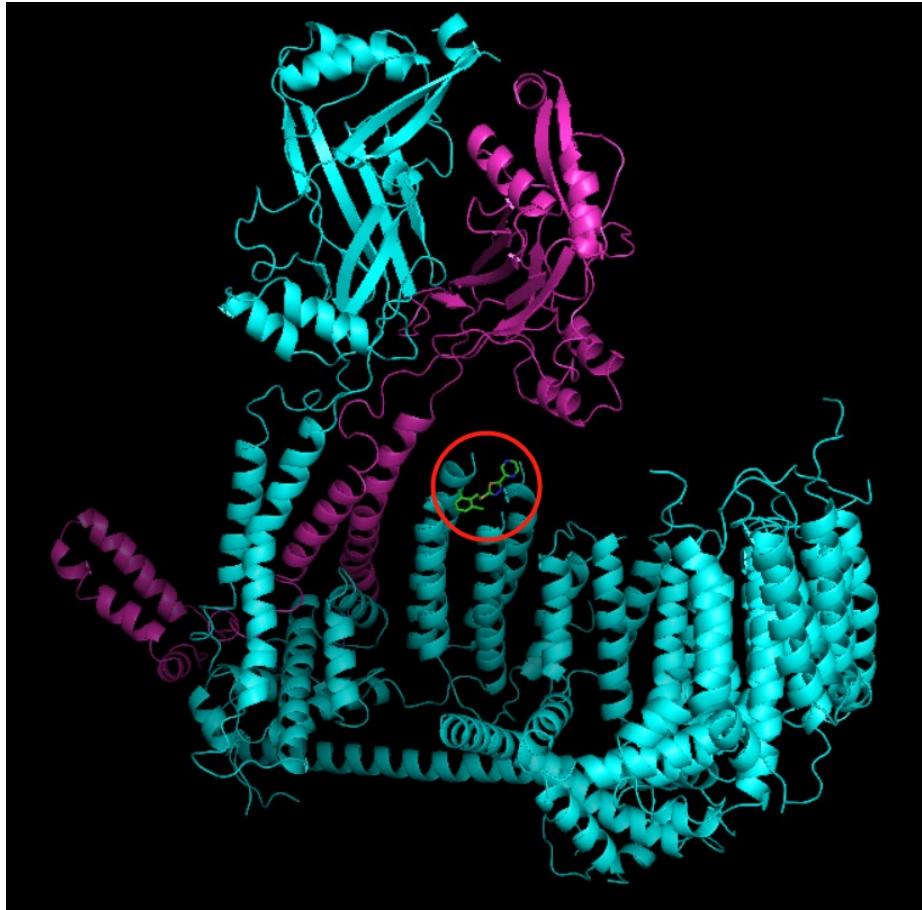
3. Dock ligand into grid box:

Genetic algorithm

4. Visualization



Result



Reference

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Thanks for your attention!