

# UNDERSTANDING PIEZO1 CHANNEL CONSERVATION ACROSS SPECIES



Chloe Randall, Dr Eulashini Chuntharpursat-Bon, Prof David Beech and Dr Antreas Kalli



umcsr@leeds.ac.uk

Leeds Institute of Cardiovascular and Metabolic Medicine, School of Medicine, University of Leeds, Leeds, LS2 9JT, UK

UNIVERSITY OF LEEDS

## SUMMARY

- Introduction** – PIEZO1 likely evolved from an early eukaryotic ancestor with homology across Metazoa differing greatly. However, the only identified conserved regions include domains lining the pore and the PFEW motif<sup>1-3</sup>.
- Aim** – To use phylogenetic comparison of full-length Animalia sequences of PIEZO1, allowing identification of structurally conserved regions relevant to function.
- Results** - Conservation of protein increases with progression to the C-terminal region, with 275 residues chemically conserved at particular positions, notably the transmembrane helical unit 7 (THU7), Latch, THU8, THU9, Anchor, pore outer helix (OH) and the C-terminal domain (CTD). Lack of conservation in C-terminal extracellular domain (CED) however.
- Future work** - There is conservation at key regions and residues, encouraging focus on these aspects in future studies. Identifying conservation of ion conductance and mechanosensitivity structural regions, as well as highlighting regions of divergent mechanisms in evolution.

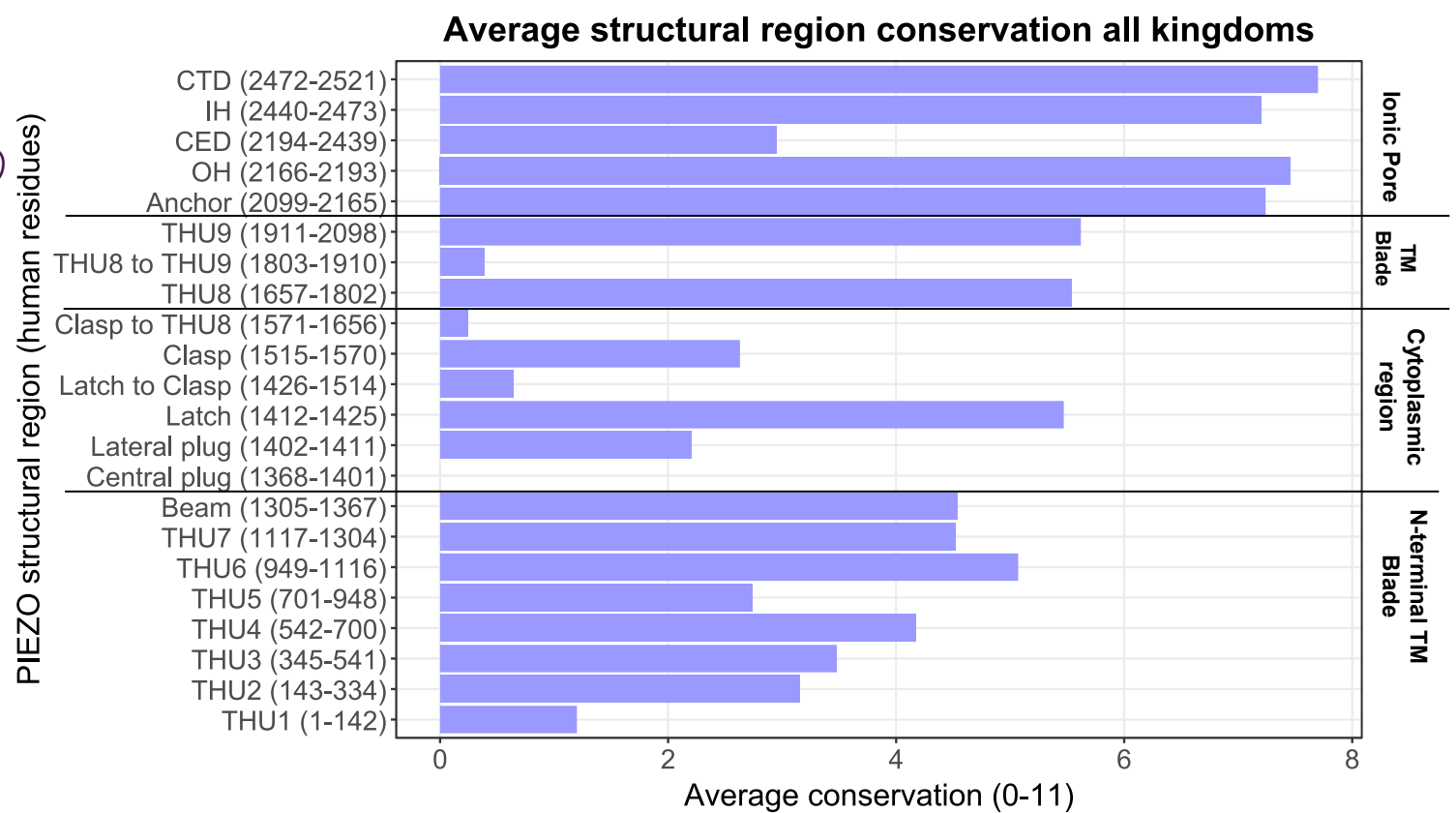
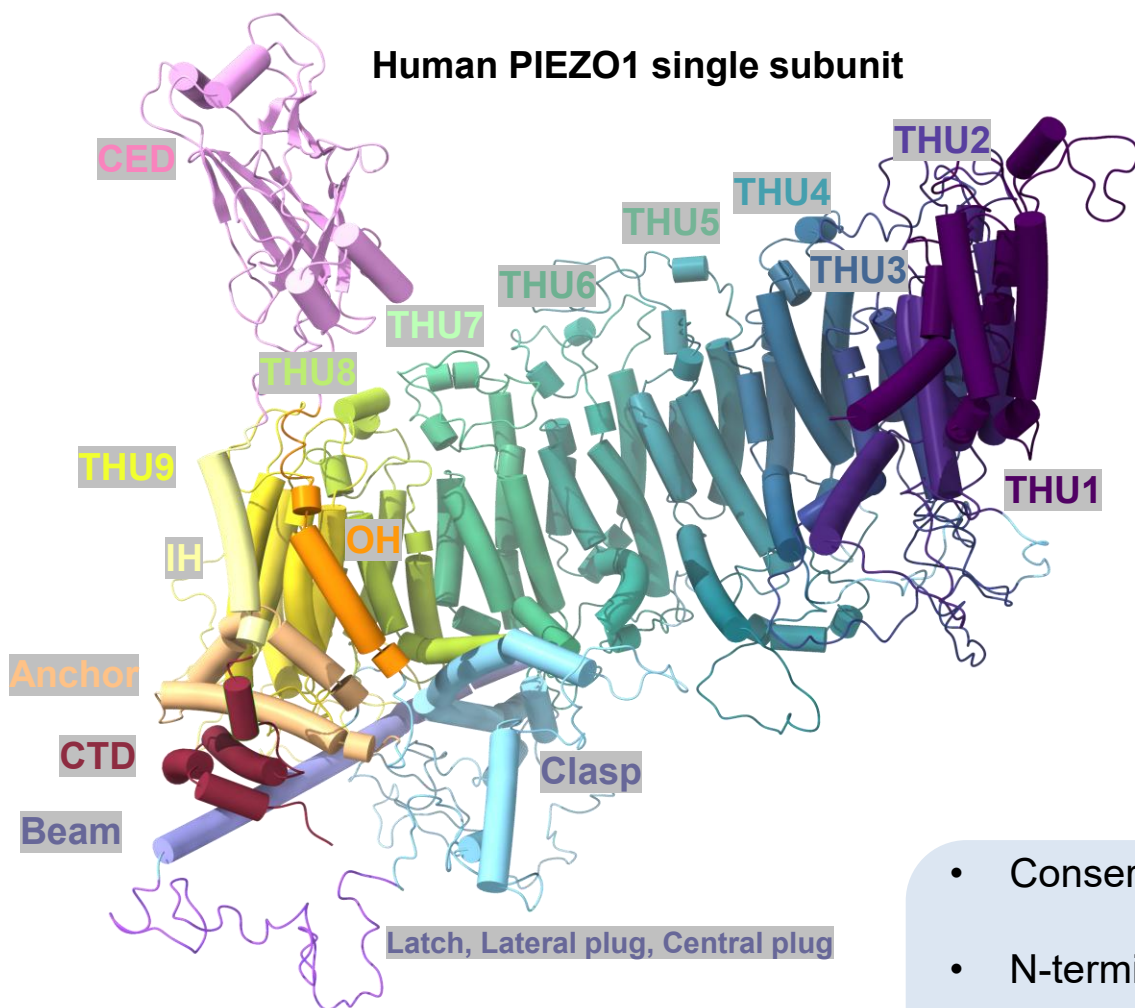
## INTRODUCTION

- PIEZO1 channels have biological relevance across organs including blood cell volume regulation, cardiovascular development and somatosensory neurons
- In early eukaryotes across multiple kingdoms, including Animalia and Protozoa likely evolved in the common eukaryotic ancestor
- The homology of PIEZO subunits among the Metazoa and Protozoa range widely in size, with ~1500 residue difference, there is consistency in the transmembrane domains lining the pore predicted and in the PFEW motif
- Noted divergence of ion selectivity seen in invertebrates lateral plug<sup>4</sup>.

## METHODOLOGY

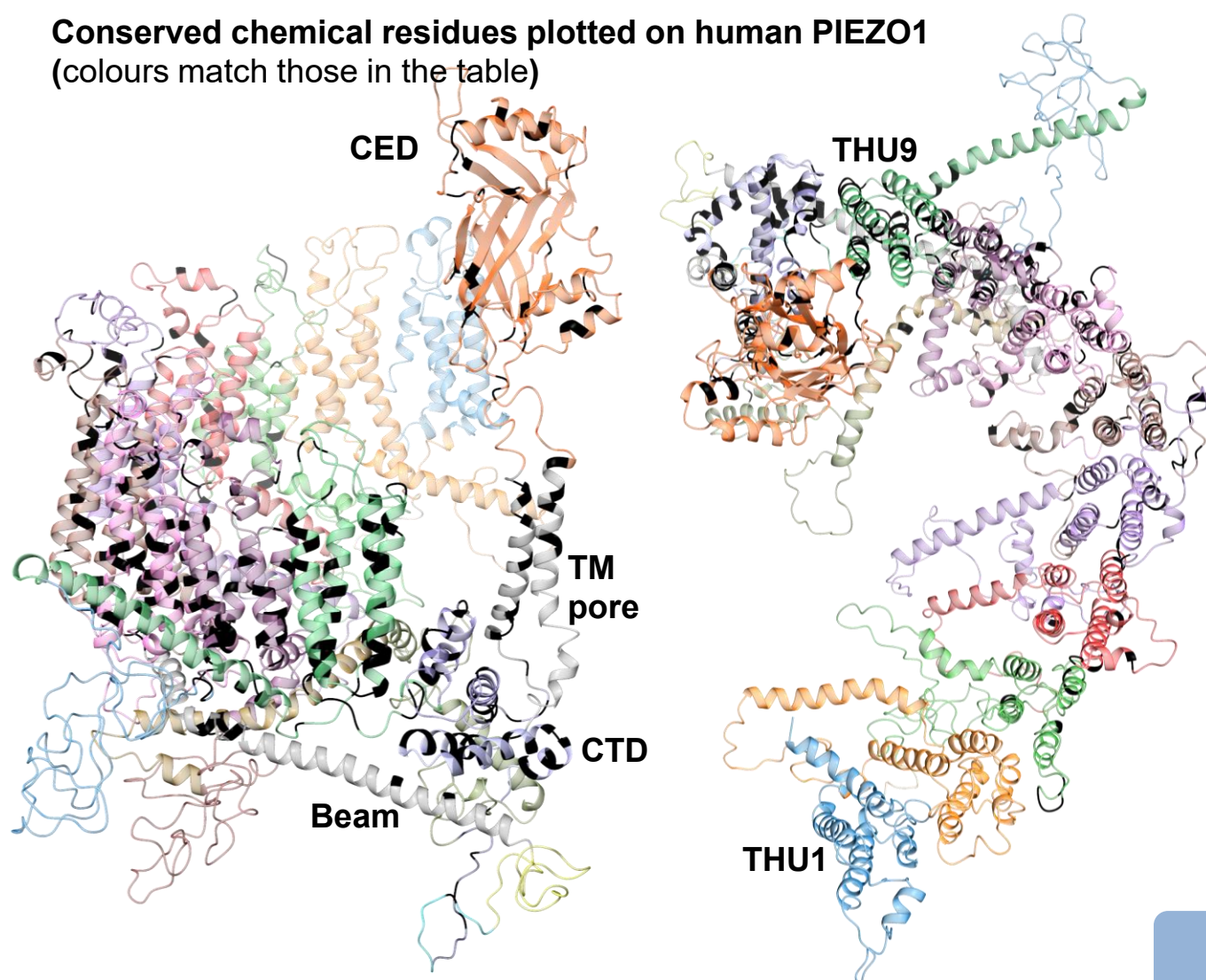
- An assembly of 246 PIEZO1/PIEZO sequences was performed using BLAST to find full-length protein sequences.
- The sequences were aligned using MAFFT multi-sequence alignment performed using EMBL-EBI.
- Using the conserved score interpreted by Jalview an average of regional conservation (0-11) was calculated using the PIEZO1 region residues

## RESULTS



- Conservation of the protein increases with progression to the C-terminus
- N-terminal blade, cytoplasmic and unstructured regions all showed low conservation (<4.5)
- Ionic pore exhibited increased conservation (+7) apart for extracellular CED
- 275 residues retained their physico-chemical properties (see table below for details)

Conserved chemical residues plotted on human PIEZO1 (colours match those in the table)



Conserved chemical regions

Region	Total conserved	Percentage of region (%)
THU3 (345-541)	10	5.10
THU4 (542-700)	8	5.06
THU5 (701-948)	13	5.26
THU6 (949-1116)	8	4.79
THU7 (1117-1304)	54	29.51
Beam (1305-1367)	5	8.06
Lateral plug (1402-1411)	1	11.11
Latch (1412-1425)	3	23.08
Latch to Clasp (1426-1514)	1	1.14
Clasp (1515-1570)	3	5.45
THU8 (1657-1802)	34	23.45
THU8 to THU9 (1803-1910)	3	2.80
THU9 (1911-2098)	48	25.67
Anchor(2099-2165)	20	30.30
OH (2166-2193)	8	29.63
CED (2194-2439)	28	11.43
IH (2440-2473)	5	15.15
CTD (2472-2521)	23	46.94
Total	275	

## CONCLUSION

- Features conserved: Latch, C-terminal blade (THU8 and THU9) and ionic pore
- CTD shows ~47% conservation of its total structure. The anchor domain and OH exhibit ~30%
- Lack of conserved residues identified in THU1-2, central plug or clasp to THU8

- There is limited conservation of the N-terminal blades potentially due to variation in force sensing requirements in alternative physiological environments
- Noticeable increase in conservation THU7, Latch, THU8, THU9, Anchor, pore outer helix (OH) and the C-terminal domain (CTD) suggesting core roles of these regions across evolutionary and species.

## Acknowledgments:

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## References:

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