Phylogeny  
• Kinome classification: Tyrosine Kinase (TK) group, Eph receptor family, A-class subgroup (tang2020ephreceptorsas pages 1-4).  
• Evolutionary relationships: clusters with EphA2, EphA7 and EphA8 in phylogenetic trees (aasheim2005characterizationofa pages 1-2); shares catalytic-site substitutions with the kinase-dead receptor EphB6 (truitt2011dancingwiththe pages 5-6).  
• Orthologs: mouse Epha10 (88 % nucleotide and 91 % amino-acid identity to human EPHA10) (aasheim2005characterizationofa pages 3-5). No additional orthologs reported in the cited literature.

Reaction Catalyzed  
ATP + [protein]-L-tyrosyl → ADP + [protein]-L-tyrosyl-phosphate (tang2020ephreceptorsas pages 1-4).  
Note: EPHA10 cannot catalyze this reaction because the VAIK, HRD and DFG motifs are replaced by VAVH, HRG and GFG, respectively (truitt2011dancingwiththe pages 5-6).

Cofactor Requirements  
Active Eph kinases require divalent cations such as Mg²⁺ or Mn²⁺ for phosphotransfer (tang2020ephreceptorsas pages 1-4). No cofactor dependence has been demonstrated for EPHA10 owing to its catalytic inactivity (truitt2011dancingwiththe pages 5-6).

Substrate Specificity  
No intrinsic substrate motif or phosphotyrosine preference has been reported for EPHA10; substrate specificity remains undefined (truitt2011dancingwiththe pages 5-6, shin2020thecatalyticallydefective pages 11-11).

Structure  
• Domain organisation: N-terminal ligand-binding domain, cysteine-rich/Sushi-EGF module, two fibronectin type-III repeats, single transmembrane helix, juxtamembrane segment, intracellular pseudokinase domain, SAM domain, and C-terminal PDZ-binding motif (unknownauthors2016…interactand pages 1-2, toracchio2024epha2incancer pages 1-2).  
• Catalytic-site substitutions: VAVH (β3-lysine region), HRG (catalytic loop) and GFG (activation loop) abolish phosphotransfer activity (truitt2011dancingwiththe pages 5-6).  
• Isoforms: full-length receptor, a transmembrane variant lacking the SAM domain, a soluble ectodomain, and additional 48 kDa, 50 kDa and 86 kDa species detected in breast cells (aasheim2005characterizationofa pages 1-2, unknownauthors2016…interactand pages 2-4).  
• Biophysical properties: intracellular regions are conformationally flexible and can bind ATP or ATP-competitive small molecules despite catalytic inactivity (liang2021theintracellulardomains pages 1-2).  
• No high-resolution crystal or cryo-EM structure has been published; current information derives from domain prediction and biophysical studies (liang2021theintracellulardomains pages 1-2).

Regulation  
• Heterodimerisation with catalytically active EphA7 leads to EPHA10 cross-phosphorylation and complex formation (unknownauthors2016…interactand pages 7-8).  
• Phosphorylated juxtamembrane tyrosines recruit SH2-domain proteins Abl, Src and Vav3 (liang2021theintracellulardomains pages 1-2).  
• EPHA10 expression enhances p38 MAPK phosphorylation (unknownauthors2016…interactand pages 1-2).  
• Alternative splicing that removes the SAM domain modulates oligomerisation potential (aasheim2005characterizationofa pages 1-2).  
• Specific phosphorylation or ubiquitination sites and the enzymes responsible have not been mapped.

Function  
• Expression patterns: high expression in testis with negligible levels in other normal adult tissues (aasheim2005characterizationofa pages 5-6). Over-expression documented in breast, pancreatic, prostate and non-small-cell lung cancers (unknownauthors2016…interactand pages 2-4, shin2020thecatalyticallydefective pages 10-11, wang2024comprehensiveanalysisof pages 6-9).  
• Ligand binding: highest affinity for ephrin-A3; lower affinity for ephrin-A1, A2, A4 and A5 (aasheim2005characterizationofa pages 5-6, truitt2011dancingwiththe pages 5-6).  
• Interacting partners: EphA7 (heterodimerisation) (unknownauthors2016…interactand pages 7-8); SH2-adaptors Abl, Src and Vav3 via phosphorylated JM region (liang2021theintracellulardomains pages 1-2).  
• Signalling outputs: increased p38 activation (unknownauthors2016…interactand pages 1-2) and up-regulation of PD-L1 expression contributing to immune evasion in tumour cells (shin2020thecatalyticallydefective pages 10-11).

Inhibitors  
Neutralising monoclonal antibodies and antibody–drug conjugates targeting EPHA10 have been generated and evaluated in pre-clinical cancer models (shin2020thecatalyticallydefective pages 10-11).

Other Comments  
• Breast cancer: EPHA10 over-expression correlates with lymph-node metastasis (anderton2021theroleof pages 5-6); nuclear localisation in invasive breast cells is suppressed by the metastasis inhibitor EphB6 (unknownauthors2016…interactand pages 7-8).  
• Pancreatic cancer: EPHA10 promotes tumourigenesis in cell and xenograft models (shin2020thecatalyticallydefective pages 10-11).  
• NSCLC: high EPHA10 transcript levels associate with poor prognosis and altered immune infiltration (wang2024comprehensiveanalysisof pages 6-9).  
• Isoform-specific modulation of E-cadherin/β-catenin complexes reported in breast cancer (buckens2020theroleof pages 31-34).

References

1. (aasheim2005characterizationofa pages 1-2): H. Aasheim, S. Patzke, H. Hjorthaug, and E. Finne. Characterization of a novel eph receptor tyrosine kinase, epha10, expressed in testis. Biochimica et biophysica acta, 1723 1-3:1-7, May 2005. URL: https://doi.org/10.1016/j.bbagen.2005.01.011, doi:10.1016/j.bbagen.2005.01.011. This article has 101 citations.
2. (anderton2021theroleof pages 5-6): Meg Anderton, Emma van der Meulen, M. Blumenthal, and Georgia Schäfer. The role of the eph receptor family in tumorigenesis. Cancers, Jan 2021. URL: https://doi.org/10.3390/cancers13020206, doi:10.3390/cancers13020206. This article has 67 citations and is from a peer-reviewed journal.
3. (shin2020thecatalyticallydefective pages 10-11): Won‐Sik Shin, Mi Kyung Park, Young Hun Lee, Kyung Woo Kim, Ho Lee, and Seung‐Taek Lee. The catalytically defective receptor protein tyrosine kinase epha10 promotes tumorigenesis in pancreatic cancer cells. Cancer Science, 111:3292-3302, Jul 2020. URL: https://doi.org/10.1111/cas.14568, doi:10.1111/cas.14568. This article has 21 citations and is from a peer-reviewed journal.
4. (truitt2011dancingwiththe pages 5-6): L. Truitt and A. Freywald. Dancing with the dead: eph receptors and their kinase-null partners. Biochemistry and cell biology = Biochimie et biologie cellulaire, 89 2:115-29, Feb 2011. URL: https://doi.org/10.1139/o10-145, doi:10.1139/o10-145. This article has 78 citations.
5. (unknownauthors2016…interactand pages 1-2): … interact and differentially co-localize in normal breast and breast carcinoma cell lines, and the co-localization pattern is altered in EPHB6-expressing MDA-MB-231 …
6. (wang2024comprehensiveanalysisof pages 6-9): Anqi Wang, Jianjie Zhu, Yue Li, Min Jiao, Saiqun Zhang, Zong-Li Ding, Jianyang Huang, and Zeyi Liu. Comprehensive analysis of epha10 as a predictor of clinical prognosis and immune checkpoint therapy efficacy in non-small cell lung cancer. Scientific Reports, Aug 2024. URL: https://doi.org/10.1038/s41598-024-70466-8, doi:10.1038/s41598-024-70466-8. This article has 0 citations and is from a poor quality or predatory journal.
7. (aasheim2005characterizationofa pages 3-5): H. Aasheim, S. Patzke, H. Hjorthaug, and E. Finne. Characterization of a novel eph receptor tyrosine kinase, epha10, expressed in testis. Biochimica et biophysica acta, 1723 1-3:1-7, May 2005. URL: https://doi.org/10.1016/j.bbagen.2005.01.011, doi:10.1016/j.bbagen.2005.01.011. This article has 101 citations.
8. (aasheim2005characterizationofa pages 5-6): H. Aasheim, S. Patzke, H. Hjorthaug, and E. Finne. Characterization of a novel eph receptor tyrosine kinase, epha10, expressed in testis. Biochimica et biophysica acta, 1723 1-3:1-7, May 2005. URL: https://doi.org/10.1016/j.bbagen.2005.01.011, doi:10.1016/j.bbagen.2005.01.011. This article has 101 citations.
9. (liang2021theintracellulardomains pages 1-2): Lung-Yu Liang, Michael Roy, Christopher R. Horne, Jarrod J. Sandow, Minglyanna Surudoi, Laura F. Dagley, Samuel N. Young, Toby Dite, Jeffrey J. Babon, Peter W. Janes, Onisha Patel, James M. Murphy, and Isabelle S. Lucet. The intracellular domains of the ephb6 and epha10 receptor tyrosine pseudokinases function as dynamic signalling hubs. Biochemical Journal, 478:3351-3371, Sep 2021. URL: https://doi.org/10.1042/bcj20210572, doi:10.1042/bcj20210572. This article has 18 citations and is from a domain leading peer-reviewed journal.
10. (shin2020thecatalyticallydefective pages 11-11): Won‐Sik Shin, Mi Kyung Park, Young Hun Lee, Kyung Woo Kim, Ho Lee, and Seung‐Taek Lee. The catalytically defective receptor protein tyrosine kinase epha10 promotes tumorigenesis in pancreatic cancer cells. Cancer Science, 111:3292-3302, Jul 2020. URL: https://doi.org/10.1111/cas.14568, doi:10.1111/cas.14568. This article has 21 citations and is from a peer-reviewed journal.
11. (tang2020ephreceptorsas pages 1-4): F. Tang, Deodate Davis, W. Arap, R. Pasqualini, and F. Staquicini. Eph receptors as cancer targets for antibody-based therapy. Advances in cancer research, 147:303-317, Jun 2020. URL: https://doi.org/10.1016/bs.acr.2020.04.007, doi:10.1016/bs.acr.2020.04.007. This article has 10 citations and is from a peer-reviewed journal.
12. (unknownauthors2016…interactand pages 2-4): … interact and differentially co-localize in normal breast and breast carcinoma cell lines, and the co-localization pattern is altered in EPHB6-expressing MDA-MB-231 …
13. (unknownauthors2016…interactand pages 7-8): … interact and differentially co-localize in normal breast and breast carcinoma cell lines, and the co-localization pattern is altered in EPHB6-expressing MDA-MB-231 …
14. (buckens2020theroleof pages 31-34): Oscar J Buckens, Btissame El Hassouni, Elisa Giovannetti, and Godefridus J Peters. The role of eph receptors in cancer and how to target them: novel approaches in cancer treatment. Expert Opinion on Investigational Drugs, 29:567-582, May 2020. URL: https://doi.org/10.1080/13543784.2020.1762566, doi:10.1080/13543784.2020.1762566. This article has 70 citations and is from a peer-reviewed journal.
15. (toracchio2024epha2incancer pages 1-2): Lisa Toracchio, Marianna Carrabotta, Caterina Mancarella, Andrea Morrione, and Katia Scotlandi. Epha2 in cancer: molecular complexity and therapeutic opportunities. International Journal of Molecular Sciences, 25:12191, Nov 2024. URL: https://doi.org/10.3390/ijms252212191, doi:10.3390/ijms252212191. This article has 4 citations and is from a peer-reviewed journal.