Phylogeny  
• Orthologs are documented in Homo sapiens, Mus musculus, Rattus norvegicus, Danio rerio, Fugu rubripes, Drosophila melanogaster, Anopheles gambiae, Caenorhabditis elegans, Ciona intestinalis, Amphimedon queenslandica and Hydra magnipapillata (nalbant2005fam20anevolutionarily pages 16-17).  
• Single Fam20B-like enzymes in sponge and hydra place Fam20B at the ancestral root of the Fam20 family (zhang2018structureandevolution pages 6-7).  
• Subsequent duplications produced monomeric Fam20B, dimeric protein kinase Fam20C and the catalytically inactive paralog Fam20A (zhang2018structureandevolution pages 9-10).  
• In the human kinome, FAM20B resides in the secretory-pathway Fam20 subfamily within the atypical “Other” kinase group (tagliabracci2013phosphorylationofsubstrates pages 1-2).

Reaction Catalyzed  
ATP + GlcAβ1-3Galβ1-3Galβ1-4Xylβ1-O-Ser-(core protein) ⇌ ADP + GlcAβ1-3Galβ1-3Galβ1-4Xyl-2-O-phosphate-β1-O-Ser-(core protein) (tagliabracci2016methodstopurify pages 3-7).

Cofactor Requirements  
Catalysis requires Mn²⁺; activity with physiological Mg²⁺ is markedly reduced (xiao2013crystalstructureof pages 1-3, zhang2018structureandevolution pages 10-11).

Substrate Specificity  
The enzyme phosphorylates the Galβ1-4Xylβ1 disaccharide within the proteoglycan linker and does not act on the Ser-X-Glu motifs preferred by Fam20C (xiao2013crystalstructureof pages 1-3, zhang2018structureandevolution pages 7-8).

Structure  
• An N-terminal signal peptide directs a single lumenal kinase domain (tagliabracci2013phosphorylationofsubstrates pages 1-2).  
• Crystal structures of Fam20B orthologs (e.g., PDB 5XOO, 6XBO, 6XBP) show a bilobal kinase fold capped by an insertion domain that forms a dedicated saccharide-binding pocket (worby2021theabcsof pages 3-6, zhang2018structureandevolution pages 7-8).  
• Key catalytic elements: Lys321 (VAIK), Glu149 (αC), Asp299 (HRD-like), and a DNH metal-binding motif that coordinates Mn²⁺ in place of the canonical DFG (zhang2018structureandevolution pages 7-8, tagliabracci2013phosphorylationofsubstrates pages 1-2).  
• The enzyme functions as a monomer both in solution and in crystal lattices (zhang2018structureandevolution pages 9-10).  
• Mn²⁺ and ATP bind in the active site adjacent to the saccharide pocket, completing the catalytic configuration (xiao2013crystalstructureof pages 1-3).

Regulation  
• No confirmed post-translational modifications of FAM20B have been reported (worby2021theabcsof pages 3-6).  
• Activity is counteracted by the xylose-2-phosphatase XYLP; gain-of-function mutations that prevent dephosphorylation lead to sustained xylose phosphorylation and intracellular accumulation of GAG-free proteoglycans (barre2025fam20bgainoffunctionblocks pages 17-18).

Function  
• Broad expression in hematopoietic and other tissues across metazoans (nalbant2005fam20anevolutionarily pages 16-17).  
• Xylose 2-O-phosphorylation by FAM20B enables efficient B3GAT3-mediated glucuronyl transfer, driving heparan- and chondroitin-sulfate chain elongation (costa2024gingivalproteomicsreveals pages 20-21).  
• Neural-crest-specific knockout in mice causes cleft palate (chen2023deficiencyoffam20bcatalyzed pages 15-16).  
• Cartilage-specific inactivation results in chondrosarcoma and delayed ossification (ma2016inactivationoffam20b pages 10-11).  
• Gain-of-function variants impair GAG synthesis and suppress glioblastoma cell proliferation and migration (barre2025fam20bgainoffunctionblocks pages 17-18).  
• Functional interplay with B3GAT3 and XYLP situates FAM20B in the core proteoglycan linker-modification module (tagliabracci2016methodstopurify pages 3-7).

Other Comments  
• Biallelic truncating mutations cause lethal neonatal short-limb dysplasia resembling Desbuquois dysplasia (kuroda2019anovelgene pages 1-2).

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