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Review Article

Beyond Ion Channels: Emerging Roles of Fgf12 in Cellular Regulation and Cancer Progression

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Abstract:

Fibroblast growth factor 12 (FGF12), a member of the intracellular fibroblast growth factor homologous factor (FHF) subfamily, has been widely studied for its role in the modulation of voltage- gated ion channels. However, recent studies suggest that FGF12 possesses various cellular function beyond ion channel regulation, particularly in cancer progression. Accumulating evidence indicates that the upregulation of FGF12 is associated with tumor survival, therapeutic resistance, and poor prognosis through signaling pathways independent of its canonical ion channel interactions. This review summarizes the current understanding of FGF12's non-canonical functions, highlights its emerging roles in cellular regulation, and discusses its potential mechanism in oncogenic progression. Understanding these novel functions may provide a new aspect for therapeutic targeting of FGF12 in malignancies.

Keywords: fibroblast growth factor 12 (FGF12); cellular regulation; cancer progression

1. Introduction

The fibroblast growth factor (FGF) family is a large group of cell-signaling proteins that regulate a vast array of biological processes, including embryonic development, brain patterning, limb development, and tissue repair [1]. Within this family, a non-canonical subgroup known as the fibroblast growth factor homologous factors (FHFs, also called the FGF11 subfamily) has attracted increasing interest [2]. Unlike canonical FGFs, which typically act in an autocrine or paracrine manner to interact with FGF receptors (FGFRs), FHFs mainly act in an intracellular manner [3]. Fibroblast growth factor 12 (FGF12) is one of the four members in the FHF subfamily [2]. The most extensively studied function of FGF12 is its modulation of voltage-gated sodium channels [4]. Early studies demonstrated that FGF12 associates with tetrodotoxin-resistant sodium channels, influencing their gating and kinetics [5]. Subsequent work has firmly established FHFs as key regulators of excitability in neurons and cardiomyocytes through direct binding to ion channels [6,7]. Beyond its ion channel-related functions, emerging evidence suggests that FGF12 might participate in various cellular processes, including intracellular signaling pathways, transcriptional activity, and cancer progression [4]. For instance, FGF12 has been shown to interact with a modulator of the nuclear factor-κB (NF-κB) pathway [8]. Also, increasing studies have demonstrated its relationship with ribosomal biogenesis [9,10]. Notably, dysregulation of FGF12 expression has been observed in several types of cancer, including esophageal squamous cell carcinoma (ESCC), gastric cancer, and others, implying a potential contribution to tumor initiation and progression [4]. Moreover, emerging evidence suggests that FGF12 is significantly upregulated in a highly aggressive type of prostate cancer, treatment-induced neuroendocrine prostate cancer (t-NEPC), pointing toward previously unrecognized regulatory axes [11]. These findings highlight the importance of examining FGF12 from a broader biological perspective, especially in cancer studies. Despite these observations, the mechanisms by which FGF12 contributes to cancer remain far from fully understood. Although FGF12 was long considered an exclusively intracellular protein lacking secretion signals, recent studies have challenged this view by demonstrating that FGF12 can, under certain cellular contexts, be released and interact with FGFRs to promote anti-apoptotic MEK/ERK signaling [12,13]. Nevertheless, these observations appear to be context-dependent, and the extent of FGF12 contribute to tumor biology still remains unclear. Additionally, FGF12 displays a diverse subcellular distribution, including cytoplasmic, perinuclear, and nucleolar localization, and interacts with multiple protein partners ranging from ion channels to ribosome biogenesis factors [4]. How these molecular interactions converge to influence oncogenic processes,

such as proliferation, survival, lineage plasticity, or therapy resistance, remains an open question. Moreover, from a translational perspective, therapeutic targeting of FGF12 also remains an unmet challenge. Current FGF-directed therapies primarily inhibit extracellular FGF-FGFR signaling, yet such strategies are unlikely to affect intracellular, receptor-independent functions of FGF12 [14]. Thus, defining the molecular mechanisms of FGF12 in cancer is not only biologically important but also essential for identifying actionable targets and informing the development of novel therapeutic strategies. In this review, we summarize current knowledge of FGF12's non-canonical roles, with particular emphasis on its emerging functions in cancer biology. By moving beyond its well-established role as an ion channel modulator, we aim to provide a comprehensive view of FGF12 as a multifunctional protein with potential implications for oncogenesis, tumor progression, and therapeutic targeting.

2. Molecular Characteristics and Functions of Fgf12

The human FGF12 gene (NCBI GenBank: NT_011651.17) is located on chromosome 3q29, as initially determined by Southern blot hybridization using rodent–human hybrid cell lines [2] and later refined by fluorescence in situ hybridization (FISH) [15]. Genomic sequencing established that FGF12 consists of five coding exons and four introns [16]. Two independent transcription start sites located upstream of exon 1 give rise to alternative first exons (1a and 1b), resulting in two major isoforms, FGF12a and FGF12b [16]. At the protein level, both isoforms possess the conserved β-trefoil fold similar to other FGFs; however, they do not contain the classical N-terminal nuclear localization sequence (NLS) as other FGFs [17]. Nevertheless, the longer FGF12a isoform contains clusters of basic residues within exon 1a, which may function as NLS [18], while FGF12b lacks this N-terminal region and shows a more cytosolic, membrane-proximal distribution [17]. These structural differences contribute to the diverse subcellular localization patterns reported for FGF12. FGF12b is preferentially localized in the cytoplasm, where it binds and modulates voltage-gated sodium channels. In contrast, FGF12a can be secreted out from the cells and interacts with FGFR through an unconventional manner, which involves the A1 subunit of Na+/K+ ATPase (ATP1A1) [19]. This dual localization suggests that FGF12 serves as a context-dependent signaling adaptor, integrating distinct molecular networks depending on its isoform expression and spatial distribution. Beyond its classical interactions with voltage-gated sodium channels (Figure 1A) [5–7,20,21], an increasing number of studies have uncovered a broader set of protein partners of FGF12, suggesting its multifunctional roles in cellular regulation and cancer progression. Early studies had demonstrated the association of FGF12 with MAPK scaffold protein, islet-brain 2 (IB2), in the adult brain to help recruitment of p38 in MAPK pathway (Figure 1C) [3,22]. This positions its role in stress- response and proliferation-associated kinase networks. A study later demonstrated the binding of FGF12 and NF-κB essential modulator (NEMO), a central regulator of the NF-κB pathway, enabling FGF12 to attenuate NF-κB activation and influence inflammatory or survival-associated transcriptional programs (Figure 1D) [8]. More recently, proteomic analyses have expanded the functional role of FGF12 even further to its secretion and interaction with FGFR (Figure 1B) [12,13,19], which was once thought to be unable before [17,23]. FGF12 is found to be secreted from cells in a context-dependent manner, which is sufficient to activate FGFR activation, initiate the downstream signaling cascade, and protect cells from apoptosis [12,13,19]. Moreover, several studies demonstrated the involvement of FGF12 in the ribosomal biogenesis process (Figure 1F). FGF12 was found within nucleolar protein complexes, interacting with NOLC1 and TCOF1, two essential regulators of ribosomal biogenesis [9]. The protein interaction between galectin-1 and FGF12 was shown to block FGF12 secretion, subsequently affecting the assembly of the FGF12-containing ribosomal biogenesis complex [10]. This molecular interaction further highlights its multi-layered regulation role in both intracellular and extracellular spaces. Taken together, the molecular profile of FGF12 reveals a highly pleiotropic protein that operates across multiple cellular compartments, including the plasma membrane, cytosol, nucleus, and extracellular space. Its functions across regulation of ion channel dynamics, kinase signaling, inflammatory pathways, growth factor receptor activation, and ribosomal biogenesis. Such multifunctionality provides a compelling mechanistic basis for its emerging significance in cancer progression and highlights the need for deeper investigation into its tumor-associated signaling programs.

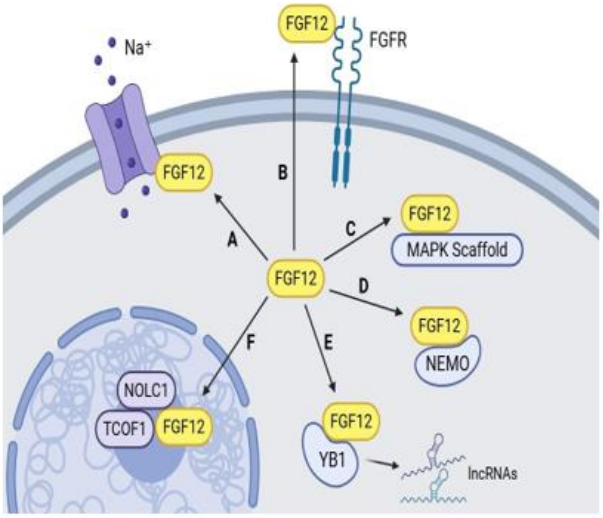

Figure 1: Multifunctional Roles of FGF12 in Cellular Physiology. (A) FGF12 binds directly to voltage-gated sodium channels and modulates channel gating and cellular excitability. (B) FGF12 can be released from cells and engage FGFRs to activate downstream pro-survival signaling pathways. (C) FGF12 interacts with MAPK scaffold proteins, shaping MAPK network architecture relevant to cell proliferation.

(D) FGF12 associates with NEMO, altering NF-κB activation in response to cellular stress. (E) FGF12 interacts with YB1 and promotes YB1- dependent stabilization of oncogenic lncRNAs. (F) FGF12 interacts with NOLC1/TCOF1 in nucleus and nucleolus, forming complexes necessary for ribosomal biogenesis and global translational capacity. Created with BioRender.com.

3. Fgf12 in Cancer Biology

3.1. Association Between Fgf12 and Cancer

Accumulating transcriptomic, proteomic, and clinical evidence indicates that FGF12 is upregulated across various human cancers, suggesting its broad oncogenic relevance (Table 1). At the transcriptomic level, multiple large-scale sequencing studies have independently highlighted FGF12 as a gene associated with poor prognosis. In diffuse large B-cell lymphoma (DLBCL), FGF12 was included in a validated 14-gene prognostic signature, where its elevated expression contributes to a high-risk score associated with inferior survival outcomes [24]. Similarly, in early-stage non- small cell lung cancer, a TCGA-based genomic analysis identified the copy-number alterations (CNA) of FGF12 among a small set of genetic events, which were significantly associated with reduced overall survival, suggesting that disruption of FGF12 dosage may contribute to early-stage lung tumor progression or aggressiveness [25]. Single-cell RNA-sequencing of low-grade endometrial stromal sarcoma (LG-ESS) further revealed that FGF12 is selectively enriched in a malignant tumor subpopulation, where high expression correlates with poor prognosis [26]. Moreover, genetic evidence also links FGF12 to bladder cancer susceptibility, in which a functional promoter variant (rs1464938) was shown to increase bladder cancer risk, indicating that inherited regulatory alterations of FGF12 may also contribute to carcinogenesis [27]. Proteomic evidence further supports the relevance of FGF12 in cancer biology. Large-scale data from the Human Protein Atlas and TCGA Pan-Cancer datasets indicate that FGF12 is consistently upregulated in gliomas and renal cancers, where higher expression is associated with worse clinical outcomes [28]. In esophageal squamous cell carcinoma (ESCC), integrative analysis of TCGA and GEO datasets showed that high FGF12 expression correlates strongly with advanced disease stage and poor overall survival [29]. The study further validates the high FGF12 expression by IHC staining on tissue microarrays (TMA), further supporting its potential as a prognostic cancer biomarker [29]. In gastric cancer, an early gene expression profiling study identified FGF12 among the genes significantly upregulated in tumor tissues compared with normal gastric mucosa [30]. Clinically, FGF12 was identified as part of a serum biomarker panel capable of distinguishing gastric cancer patients from healthy individuals, highlighting its promise as a non-invasive early detection marker [31]. Notably, a recent study in our lab demonstrated that FGF12 expression is highly upregulated in advanced prostate cancer states, including t-NEPC [11]. By analyses through public transcriptomic datasets across different models and IHC staining with patient cohorts, the study suggested a solid upregulation of FGF12 in t-NEPC and its role in cancer cell survival and potential drug resistance [11]. Together, these findings illustrate a consistent pattern that FGF12 upregulation is frequently associated with tumor progression, aggressive phenotypes, and worse clinical outcomes across diverse cancer types. This broad oncogenic association underscores the importance of investigating FGF12 as a potential biomarker and mechanistic contributor to cancer biology.

Tumor Type	Source / Samples	Results / Evidence	Ref.
Diffuse Large B-Cell Lymphoma	TCGA / GEO analyses	High FGF12 → high-risk score and poorer survival	[22]
Non-Small Cell Lung Cancer (NSCLC)	14-gene prognostic signature study (TCGA)	High FGF12 associated with overall survival in stage I NSCLC	[23]
Pan-Lung Cancer	Single-cell RNA-seq (cohort study)	High FGF12 in a tumor sub-population → poor prognosis	[24]
Bladder Cancer	Case-control genetic association study	FGF12 promoter variant *rs1464938* → higher bladder cancer risk	[25]
Glioma / GBM	TCGA; Human Protein Atlas	Higher FGF12 expression associated with gliomas	[26]
Renal Cancer	TCGA; Human Protein Atlas	Higher FGF12 associated with renal cancer	[26]
Esophageal Squamous Cell Carcinoma (ESCC)	TCGA / GEO analyses; Tissue microarray	High FGF12 → poor survival	[27]
Gastric Cancer	Gene-expression reanalysis; miRNA database integration	High FGF12 associated with gastric cancer patients	[28]
Gastric Cancer	Serum biomarker panel (small clinical cohort)	High FGF12 associated with gastric cancer patients	[29]
Prostate Cancer	TCGA / GEO analyses; Tissue microarray	High FGF12 → t-NEPC progression	[11]

3.2. Potential Mechanisms of Fgf12 Function in Cancer

Although accumulating evidence suggests a strong relationship between FGF12 upregulation and the development of different types of cancer, the mechanisms of FGF12 in cancer still remain limited. At the molecular level, the longer FGF12a isoform was demonstrated to be released from cells via an unconventional secretion pathway, by the assistance of the ATP1A1 [18]. Secreted FGF12a is capable of activating FGFR signaling and downstream MEK/ERK pathways to promote cell survival in recipient cells, providing a direct route of previously thought intracellular FHF to

engage in canonical receptor tyrosine kinase signaling in the tumor microenvironment (Figure 1B) [18]. These findings imply that, in some tumors, extracellular FGF12 may function in an autocrine or paracrine manner to enhance pro-survival signaling. Additionally, proteomic studies placed FGF12 in proximity to MAPK scaffold proteins (Figure 1C) [3,21]. By interacting with MAPK scaffolds, IB2, FGF12 could locally concentrate kinases such as p38 or ERK, modulating pathway amplitude or duration and thereby influencing proliferation, stress responses, or therapy sensitivity. However, direct evidence of FGF12 to interact with the MAPK pathway in cancer are still limited, which may require future study to demonstrate. Some other studies of FGF12 function also showed plausible mechanisms of it in cancer. FGF12 binds NEMO and negatively regulates NF-κB activation in neuronal models (Figure 1D) [8]. By analogy, similar interactions for FGF12 provide a plausible mechanism by which FGF12 could reprogram inflammatory and survival transcriptional outputs in cancer cells, altering cytokine responses or apoptosis thresholds. Direct evidence for FGF12-NEMO binding in tumor cells remains limited and represents an important subject for future mechanistic work. Within nucleus, FGF12 localizes to the nucleolus and forms complexes with nucleolar assembly factors NOLC1 and TCOF1 (Figure 1F). In these complexes, FGF12 appears necessary for stable assembly, linking it functionally to ribosome biogenesis [9]. Because ribosomal production and translational capacity are tightly coupled to cell growth and oncogenesis, nucleolar FGF12 has the potential to influence global protein synthesis and thus support tumor proliferation under nutrient or stress constraints. Notably, the requirement of FGF12's C-terminal region and phosphorylation state for complex formation suggests regulatory points that could be therapeutically targeted [9].

A recent study from our lab expands the role of FGF12 in cancer to its association with RNA- binding proteins and long non-coding RNAs (lncRNAs) (Figure 1E) [11]. We found that FGF12 interacts with the RNA-binding protein, YB1, a well-established oncoprotein involved in mRNA stabilization, translation control, and stress response [31]. The finding suggests that FGF12 can enhance the activity of YB1 in promoting the stabilization and expression of oncogenic lncRNAs, including NEAT1 and MALAT1, both of which are known to facilitate cancer cell proliferation, metastasis, and therapy resistance [32–34]. This FGF12-YB1-lncRNAs axis suggests that FGF12 could function as a post-transcriptional regulator that promotes tumor cell survival through modulation of RNA metabolism and gene expression networks. Taken together, these findings support a model in which FGF12 acts not merely as an ion channel regulation protein, but rather as a multifunctional cellular regulator with the capacity to rewrite transcriptional and post-transcriptional programs in cancer cells. Although current studies showing its roles in cancer are still limited, future studies dissecting the precise molecular interaction of FGF12 will be crucial for establishing its role as a bona fide oncogenic driver and potential therapeutic target.

4. Therapeutic Implications

The available data indicate that FGF12 has potential both as a biomarker and as a therapeutic target in cancer, but the evidence is still preliminary and tumor-context dependent. As mentioned before, multiple transcriptomic and proteomic studies have reported elevated FGF12 expression associated with worse clinical outcomes in specific cancers, supporting its potential use as a prognostic marker. From the therapeutic targeting perspective, several therapeutic strategies could plausibly be considered to exploit FGF12 biology. Because FGF12 was long considered an intracellular protein, classical extracellular approaches were not pursued. However, recent evidence that FGF12 can be unconventionally secreted and activate FGFR-MEK/ERK signaling opens the possibility that extracellular blockade, including FGFR inhibitors or FGF-trapping agents, could be effective [35–37]. Nevertheless, although these clinically approved therapeutic agents can engage in targeting receptor-mediated FGF12 function, they will not affect strictly intracellular functions of FGF12. For intracellular activities of FGF12, therapeutic options remain conceptual but tractable. RNA-targeting approaches, such as siRNA, could reduce FGF12 expression and are technically feasible. In addition, small molecules or peptides that disrupt critical FGF12 protein-protein interactions, such as the FGF12-YB1 interaction, could abrogate oncogenic complexes. Evidence already showed galectin-1 can bind to FGF12 in both cytosol and nucleus to block its different functions, which offers a novel angle for intervention [10]. Furthermore, targeting downstream effectors, including MAPK, NF-κB, and YB1, may offer opportunities to blunt FGF12-driven phenotypes. A recent study has shown that in non-cancer models, FGF12 can reduce stress-induced ferroptosis by activating FGFR1/MAPK/NRF2 signaling [38]. If a similar pathway is activated in cancer, small-molecule inhibitors of AMPK or modulators of NRF2 could potentially blunt FGF12's survival benefits. Although these therapeutic strategies are biologically plausible, there are substantial gaps and challenges for targeting FGF12 before clinical translation. First, the expression level of FGF12 could be low at early-stage cancer development. For example, in prostate cancer, the FGF12 expression is negative in hormone naïve prostate cancer. Only after cancer developed into more aggressive and lethal types, such as CRPC and t-NEPC, did the expression of FGF12 upregulated [11]. This fact limited the treatment utility for targeting FGF12 in cancer therapy. Second, FGF12 exists as multiple isoforms and may have context-specific interactomes and subcellular localizations, complicating the selection of a universal targeting strategy. Third, because FGF12 is involved in essential processes, such as RNA metabolism and ribosome biogenesis in cells, systemic inhibition could carry toxicity risks, particularly for tissues with high baseline levels. Finally, identifying druggable interfaces, either small-molecule binding pockets or surfaces amenable to degraders, will be technically challenging and will require detailed structural and interactome mapping. To move forward clinical application, several steps, including 1) broadened validation of FGF12 expression and prognostic value across large, well-annotated patient cohorts and multi-omics datasets, 2) mechanistic dissection of the most therapeutically relevant FGF12 interactions, such as the known FGF12-YB1-lncRNAs axis, including the structure characterization, 3) development and testing of cell-penetrant modalities, including ASOs/siRNA, small molecules, or degraders, across different in vivo models to assess efficacy and toxicity. With these steps, FGF12 could transition from an intriguing biological player to a clinically actionable target in selected cancer settings.

5. Conclusion:

FGF12 is emerging as a multifunctional regulator in cancers, far beyond its traditional role in interacting with ion channels. Evidence from transcriptomic, proteomic, and clinical studies shows that FGF12 is upregulated across diverse malignancies and often associates with aggressive disease features. At the molecular level, FGF12 participates in several cancer-relevant processes, including intracellular signaling, nucleolar function, and RNA regulation, and may also act extracellularly through unconventional secretion. Despite these advances, the mechanisms by which FGF12 contributes to tumor progression remain incompletely understood, which poses challenges for therapeutic targeting. Moving forward, systematic mechanistic dissection and validation across cancer models are needed to define its roles and therapeutic prospective. Such efforts will determine whether FGF12 can become a meaningful therapeutic target in oncology.

6. Author Contributions:

Conceptualization, Z.H. and X.D.; writing—original draft preparation, Z.H.; writing— review and editing, Z.H. and X.D.; visualization, Z.H.; supervision, X.D.; project administration, X.D. All authors have read and agreed to the published version of the manuscript.

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References

1. Beenken, A.; Mohammadi, M. (2009). The FGF family: biology, pathophysiology and therapy. Nat Rev Drug Discov 2009, 8, 235-253, doi:10.1038/nrd2792.
2. Smallwood, P.M.; Munoz-Sanjuan, I.; Tong, P.; Macke, J.P.; Hendry, S.H.; Gilbert, D.J. et.al., (1996). Nathans, J. Fibroblast growth factor (FGF) homologous factors: new members of the FGF family implicated in nervous system development. *Proc Natl Acad Sci* U S A 1996, 93, 9850-9857, doi:10.1073/pnas.93.18.9850.
3. Schoorlemmer, J.; Goldfarb, M. (2001). Fibroblast growth factor homologous factors are intracellular signaling proteins. *Curr Biol*, 11, 793-797, doi:10.1016/s0960-9822(01)00232-9.
4. Biadun, M.; Karelus, R.; Krowarsch, D.; Opalinski, L.; Zakrzewska, M. et.al., (2024).: biology and function. Differentiation, 139, 100740, doi:10.1016/j.diff.2023.100740.
5. Liu, C.; Dib-Hajj, S.D.; Waxman, S.G. (2001). Fibroblast growth factor homologous factor 1B binds to the C terminus of the tetrodotoxin-resistant sodium channel rNav1.9a (NaN). *J Biol Chem*, 276, 18925-18933, doi:10.1074/jbc.M101606200.
6. Wildburger, N.C.; Ali, S.R.; Hsu, W.C.; Shavkunov, A.S.; Nenov, M.N.et al.(2015). Quantitative proteomics reveals protein- protein interactions with fibroblast growth factor 12 as a component of the voltage-gated sodium channel .2 (nav1.2) macromolecular complex in Mammalian brain. *Mol Cell Proteomics*, 14, 1288-1300, doi:10.1074/mcp.M114.040055.
7. Seiffert, S.; Pendziwiat, M.; Bierhals, T.; Goel, H.; Schwarz, N.; van der Ven, et al.(2022). Modulating effects of FGF12 variants on Na(V)1.2 and Na(V)1.6 being associated with developmental and epileptic encephalopathy and autism spectrum disorder: *A case series. EBioMedicine* 2022, 83, 104234, doi:10.1016/j.ebiom.2022.104234.
8. König, H.G.; Fenner, B.J.; Byrne, J.C.; Schwamborn, R.F.; Bernas, T.; Jefferies. et.al., (2012). Fibroblast growth factor homologous factor 1 interacts with NEMO to regulate NF-κB signaling in neurons. *J Cell Sci*, 125, 6058-6070, doi:10.1242/jcs.111880.
9. Sochacka, M.; Karelus, R.; Opalinski, L.; Krowarsch, D.; Biadun, M. et.al., (2022). FGF12 is a novel component of the nucleolar NOLC1/TCOF1 ribosome biogenesis complex. *Cell Commun Signal*, 20, 182, doi:10.1186/s12964-022-01000-4.
10. Gędaj, A.; Chorążewska, A.; Ciura, K.; Karelus, R.; Żukowska, D.; Biaduń, M. (2024). The intracellular interplay between galectin-1 and FGF12 in the assembly of ribosome biogenesis complex. *Cell Commun Signal*, 22, 175, doi:10.1186/s12964-024-01558-1.
11. Huang, Z.; Kung, S.H.Y.; Adomat, H.; Oo, H.Z.; Forbes, C.; Hach, F.; Dong. et.al., (2025). X. FGF12 Enhances Prostate Cancer Cell Survival via the YB1-lncRNA Axis. *Cells*, 14, 1828, doi:10.3390/cells14221828.
12. Sochacka, M.; Opalinski, L.; Szymczyk, J.; Zimoch, M.B.; Czyrek, A. (2020). FHF1 is a bona fide fibroblast growth factor that activates cellular signaling in FGFR- dependent manner. *Cell Commun Signal*, 18, 69, doi:10.1186/s12964-020-00573-2.
13. Biadun, M.; Sochacka, M.; Karelus, R.; Baran, K.; Czyrek, A.(2023). M. FGF homologous factors are secreted from cells to induce *FGFR-mediated anti-apoptotic response*. Faseb , 37, e23043, doi:10.1096/fj.202300324R.
14. Zhang, P.; Yue, L.; Leng, Q.; Chang, C.; Gan, C.; Ye, T. et.al., (2024). Targeting FGFR for cancer therapy. *J Hematol Oncol*, 17, 39, doi:10.1186/s13045-024-01558-1.
15. Liu, Y.; Chiu, I.M. (1997). Assignment of FGF12, the human FGF homologous factor 1 gene, to chromosome 3q29-->3qter by fluorescence in situ hybridization. Cytogenet Cell Genet, 78, 48-49, doi:10.1159/000134625.
16. Munoz-Sanjuan, I.; Smallwood, P.M.; Nathans, J. (2000). Isoform diversity among fibroblast growth factor homologous factors is generated by alternative promoter usage and differential splicing. *J Biol Chem*, 275, 2589-2597, doi:10.1074/jbc.275.4.2589.
17. Olsen, S.K.; Garbi, M.; Zampieri, N.; Eliseenkova, A.V.; Ornitz.(2003). Fibroblast growth factor (FGF) homologous factors share structural but not functional homology with FGFs. *J Biol Chem*, 278, 34226-34236, doi:10.1074/jbc.M303183200.

18. Nakayama, F.; Yasuda, T.; Umeda, S.; Asada, M.; Imamura, T.et.al.(2011). Fibroblast growth factor-12 (FGF12) translocation into intestinal epithelial cells is dependent on a novel cell-penetrating peptide domain: involvement of internalization in the in vivo role of exogenous FGF12. *J Biol Chem* 2011, 286, 25823-25834, doi:10.1074/jbc.M110.198267.