**Table S1:** Pharmacological screen targeting pathways previously implicated in DFC development.

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| --- | --- | --- | --- | --- | --- |
| Targeted signalingpathway | Work implicating pathway in DFCs  | Selected drugand dose  | Drug mechanism  | Previous use of drug in zebrafish | Source |
| WNT-β-catenin(activation) | [35, 40, 97, 98] | 10 mM 1-Azakenpaullone (Az) | Inhibits GSK3B, which degrades β-catenin  | [99] | Sigma-Aldrich (A3734) |
| WNT-β-catenin(inhibition) | [35, 40, 97, 98] | 30 mM XAV939 | Tankyrase inhibitor stimulates β-catenin degradation | [100] | Sigma-Aldrich(X3004) |
| BMP(inhibition) | [101] | 25 mM LDN193189 | Inhibits activity of BMP receptors ALK2 and ALK3  | [102] | United States Biological(366895) |
| FGF(inhibition) | [103-106] | 25 mM SU5402 | Inhibits activity of FGF receptors  | [104] | EMD Millipore(572630) |
| TGFb(inhibition) | [29] | 60 mM SB505142 | Inhibitor of the TGF-β signaling via ALK5 | [107] | ApexBio(B2289) |
| Ca2+ flux(inhibition) | [40, 41] | 1 mM Thapsigargin(Thaps) | Inhibits sarco-endoplasmic reticulum Ca2+ ATPase pump (SERCA), leading to increased cytosolic calcium  | [40, 41] | Sigma-Aldrich(T9033) |
| Notch(inhibition) | [108, 109] | 100 mM DAPT | Inhibits g-secretase, preventing the release of Notch intracellular domain  | [110] | TOCRIS(2634) |
| mTOR(inhibition) | [111, 112] | 1 mM Rapamycin (Rap) | Inhibits mTORC1 complex | [111] | Cayman Chemical Company(13346) |
| SHH(activation) | [113] | 10 mMSmoothened agonist (SAG) | Activates smoothened receptor  | [114] | EMD Millipore(566661) |
| Ca2+ flux(inhibition) | [40, 41] | 100 mM Cyclopizionic acid (CPA) | Inhibits sarco-endoplasmic reticulum Ca2+ ATPase pump (SERCA), leading to increased cytosolic calcium  | [40, 41] | EMD Millipore(239805) |