PRKD1 inhibits TCF7L2 expression.

TCF7L2 activates CFL1 expression [11]. CD44 induces CFL1 expression [50,51]. LIMK inhibits CFL1 [52–57]. If both, SSH1L and LIMK are active, CFL1 stays unphosphorylated [58–60].

SSH1L dephosphorylates CFL1 [12,52–54,56–58,61]. LIMK phosphorylates CFL1 [12,52,53,56,58]. If SSH1L and LIMK are present, LIMK may restore phosphorylation, but the dephosphorylation of SSH1L is more pronounced [58–60].

TWIST1 upregulates CD44.
AURKA inhibits degradation of TWIST1.

LIMK is activated by dephosphorylation of PAK1, PAK4 and ROCK (downstream of RHOA) [48,53,55,59,61,64–66]. LIMK and SSH1L can build a complex that effectively dephosphorylates both [59,60].

F-actin enhances SSH1L activity [52,57,59,61]. PRKD1 phosphorylates SSH1L [52,53,61]. In the presence of PI3K, AURKA induces SSH1L expression [54,56,57]. LIMK and SSH1L can build a complex that effectively dephosphorylates both [59,60].

CFL1 and ARP2/3 work in synergy to create new branched actin fibres [58,67–72]. RHOA/ROCK/DIA pathway polymerizes F-actin (here RHOA delay) [64,73–75].

CFL1 severs F-actin [52,65,67] preferring old ADP-F-actin [58,68,76,77]. Newly formed actin fibres are built, prolonged and thus converted into old ones.

Downstream of RAC1, ARP2/3 is activated by WAVE or WASP (here by a RAC1 delay) [58,64,69].
Activating KRAS mutations are present in more than 90% of PDAC patients [3,46,78,79]. For this reason, the protein KRAS is assumed to be always active. Therefore, we modeled it as active (1).
The PI3K-pathway is one of the main effector pathways downstream of RAS [80]. CD44 receptor binding activates PI3K/AKT pathway [62,81,82].
RHOA activates PRKD1 [11,52,53,65].
PAK4 inhibits RHOA [83].
RAC1 is activated by PI3K [54,80,84]. Phosphorylated CFL1 activates RAC1 via PLD1 and DOCK (here with delay) [85].