PARATHYROID HORMONE SYNTHESIS, SECRETION AND ACTION

Parathyroid cell

Ca^{2+} → CaSR → Gi → AC → cAMP

CaSR → Gq/11 → PLCβ → IP3 → IP3R (ER) → Ca^{2+}

Calcium signaling pathway

1,25(OH)2D3 (Vitamin D) → VDR

FGF23 → FGFR1 / Klotho → ERK → Egr-1

GCM2, MafB, GATA3, SP1, RXR → DNA → PTH

PTH → Exocytosis

PTH → PTH

Target cell (e.g., kidney, bone, or cartilage)

FGF23 → FGFR1 / Klotho → ERK → +p → SGK1

Gq/11 → PLCβ → DAG, IP3 → PKC; IP3 → IP3R (ER) → Ca^{2+}

Calcium signaling pathway

PTH, PTHrP → PTH1R → Gs → AC → cAMP → PKA

PDE4D → AMP

cAMP signaling pathway

PTH1R → G12/13 → RhoGEF → RhoA → PLD

PTH1R → ARRB → Raf → +p → MEK → +p → ERK

PTH1R → Gi → MMP

HB-EGF → EGFR → ERK

ErbB signaling pathway

Kidney

SGK1 → +p → WNK1/4 → +p → CERK/SPAK → +p → NCC → Na^+, Cl^-

Enlarged TRPV-mediated Ca^{2+} influx → TRPV5 → Ca^{2+}

+p → Npt2a → $3Na^+$, Pi

+p → NHERF1

NPT2A/C internalization, degradation → Inhibition of phosphate transport

25(OH)D3 → Cyp27b1 → 1,25(OH)2D3 (Vitamin D) → Elevation in serum calcium level

Cyp24a1 → 1,24,25(OH)3D3

Endocrine and other factor-regulated calcium reabsorption

Bone

Wnt signaling pathway

MEF2 → DNA → Sclerostin → Bone formation

Nur1 → DNA → FGF23 → Regulation of serum phosphate and vitamin D levels

+p αNAC → αNAC / JunD → DNA → Bglap2, Lrp6 → Regulation of bone mass

+p CREB → DNA → RANKL → Bone resorption; Bcl-2, p21, c-fos → Anti-apoptosis

Osteoclast differentiation

c-fos → +p cathepsin K → DNA → MMP13 → Bone resorption

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