Fructus Ligustri lucidi (FLL) pathway-overlap chart

Overlap between pathways reported for Fructus Ligustri lucidi / Ligustri Lucidi Fructus and pathways involved in mandibular condylar cartilage, jaw growth, and bone remodeling.

Overlap grade	Meaning	Use in the chart
Strong	Same named pathway or endpoint appears in both FLL bone literature and condylar/jaw growth-remodeling literature.	Direct pathway match.
Partial	Shared biological axis, but the overlap is through a broader signaling layer, mineralization, inflammation, or downstream ossification.	Mechanistic bridge.
Some	General endocrine, antioxidant, systemic bone-quality, or adjacent cartilage-growth relevance.	Background overlap.

Condensed overlap map

Grade	Pathways / axes	Overlap type
Strong	RANKL-RANK/TRAF6-NF-kB/MAPK-NFATc1; OPG/RANKL/cathepsin K; Wnt/beta-catenin; RUNX2 osteogenesis	Direct shared remodeling or osteogenic pathways.
Partial	PI3K/Akt-RUNX2/OPN; MAPK/Akt; Nox4/ROS/NF-kB; PTH/FGF23/VitD/VDR/CaSR; BMP/Smad/Runx2; MMP-mediated ECM turnover	Shared bone/cartilage remodeling layers with broader or adjacent mapping.
Some	ER-alpha/ER-beta; Nrf2/HO-1; ferroptosis; gut microbiota/TMAO/Sirt6; Ihh/PTHrP/Sox9 cartilage axis	Background endocrine, stress, systemic, or adjacent cartilage-growth overlap.

Highest-overlap pathway cluster

Cluster	FLL side	Jaw / condyle side
Bone resorption control	RANKL cascade, TRAF6, c-Fos, NFATc1, TRAP, CTSK, MMP-9, OPG/RANKL	Osteoclastogenesis, resorption, matrix turnover, subchondral bone remodeling
Bone formation / ossification	PI3K/Akt, RUNX2, OPN, Wnt/beta-catenin, BMP/Smad	Osteoblast differentiation, chondrocyte maturation, mineralization, endochondral ossification
Systemic bone support	PTH/FGF23/VitD/VDR/CaSR, calcium transport, oxidative stress axes	Mineral balance, bone quality, remodeling under loading/inflammatory stress

Detailed pathway-overlap chart

Strong and partial overlap rows.

FLL-modulated pathway / axis	FLL modulation reported	Condylar / jaw growth-remodeling pathway	Overlap reason	Grade
RANKL -> RANK/TRAF6 -> NF-kB/MAPK -> c-Fos/NFATc1 -> TRAP/CTSK/MMP-9	FLL ethanol extract plus oleanolic acid and ursolic acid suppressed RANKL-induced osteoclast formation, TRAP activity, TRAF6, c-Fos, NFATc1, CTSK, and MMP-9 in RAW264.7 cells. [2]	Jaw and condylar remodeling use osteoclast differentiation, matrix degradation, and subchondral bone turnover during growth adaptation, loading response, and TMJ remodeling. [6,7]	Same osteoclast-resorption cascade appears on both sides.	**Strong**
OPG/RANKL/cathepsin K balance	FLL bone literature repeatedly reports regulation of OPG/RANKL/cathepsin K and related osteoblast-osteoclast communication. [1,3]	OPG/RANKL is listed among factors involved in mandibular condylar growth and remodeling; cathepsin K is a resorption marker tied to osteoclast activity. [6,8]	Direct coupling-axis overlap between bone formation cells and bone resorption cells.	**Strong**
Canonical Wnt/beta-catenin signaling	FLL studies in osteoporosis models include canonical Wnt/beta-catenin regulation as part of bone-quality preservation. [1,4]	MCC studies and reviews identify Wnt signaling among pathways involved in condylar cartilage growth, ossification, and remodeling. [5,7]	Shared growth/remodeling pathway linking osteogenesis, chondrocyte maturation, and bone adaptation.	**Strong**
RUNX2 / osteogenic differentiation	FLL promoted osteogenic differentiation of BMSCs with increased RUNX2 and OPN through PI3K/Akt-related signaling. [3]	RUNX2 appears in MCC growth-remodeling literature, especially chondrocyte maturation, mineralization, ossification, and mandibular condyle bone formation. [5,6]	Shared osteogenic-differentiation endpoint.	**Strong**
PI3K/Akt -> RUNX2/OPN	Network pharmacology, molecular docking, and in vitro validation link FLL-mediated BMSC osteogenesis to AKT1 and PI3K/Akt activation. [3]	Condylar growth includes osteogenic differentiation after cartilage maturation and matrix mineralization; PI3K/Akt is a broad survival and differentiation pathway. [5]	Clear bone-formation overlap; condylar specificity comes through the osteogenic phase.	**Partial**
MAPK/Akt signaling	FLL effects on osteoblastic cells include OPG/RANKL changes linked with MAPK and AKT signaling. [1]	MAPK/Akt operate downstream of mechanical loading, growth factors, and cell differentiation signals in cartilage and bone remodeling contexts. [5,7]	Shared intracellular signaling layer, but broader than one specific jaw pathway.	**Partial**
Nox4/ROS/NF-kB oxidative-stress axis	FLL aqueous extract is summarized as regulating Nox4/ROS/NF-kB in bone metabolism studies. [1]	NF-kB, oxidative stress, inflammation, and MMP activity are involved in TMJ degeneration, remodeling, and matrix turnover. [7]	Stress-remodeling overlap through inflammatory and matrix-turnover signaling.	**Partial**

Detailed pathway-overlap chart - continued

Partial and some overlap rows.

FLL-modulated pathway / axis	FLL modulation reported	Condylar / jaw growth-remodeling pathway	Overlap reason	Grade
PTH / FGF23 / 1,25(OH)2D3 / VDR / CaSR / calcium transport	FLL studies report effects on calcium balance and vitamin D-related mineral metabolism, including PTH/FGF23/1,25(OH)2D3/CaSR. [1]	Jaw and condylar ossification require mineral homeostasis; the condyle also uses PTHrP in cartilage proliferation/differentiation control. [6,9]	Mineralization and endocrine-bone metabolism overlap.	Partial
BMP/Smad/Runx2 osteogenesis	Ligustri Lucidi Fructus osteoporosis work has identified BMP-Smad/Runx2-related osteogenic mechanisms, especially in processed FLL research. [10]	BMP/TGF-beta and RUNX2 are core MCC growth-remodeling pathways tied to differentiation, hypertrophy, and ossification. [5,7]	Osteogenic and cartilage-to-bone transition overlap.	Partial
MMP-mediated extracellular matrix turnover	FLL ethanol extract suppressed MMP-9 in RANKL-induced osteoclastogenesis. [2]	MCC growth-remodeling literature emphasizes ECM organization and MMP activity during cartilage maturation, remodeling, and loading response. [5,7]	Shared matrix-remodeling enzyme layer.	Partial
ER-alpha / ER-beta signaling	FLL pharmacology reviews include estrogen receptor-related bone effects. [1]	Condylar cartilage and TMJ remodeling vary by age and sex; hormone-mediated signaling appears in MCC remodeling literature. [5,7]	Hormonal bone-remodeling context overlap.	Some
Nrf2/HO-1 and ferroptosis-related signaling	Recent FLL bone studies report Nrf2/HO-1 and ferroptosis-linked protection in osteoporosis models. [11]	Oxidative stress and cell-survival pathways contribute to cartilage/bone homeostasis and TMJ remodeling under stress. [7]	General stress-resilience overlap.	Some
Gut microbiota / TMAO / Sirt6 / oxidative stress	FLL bone-quality studies include gut microbiota diversity, oxidative stress, TMAO, and Sirt6 changes. [12]	This connects to systemic bone quality and inflammatory tone, which can influence skeletal remodeling capacity. [1,7]	Systemic bone-homeostasis overlap.	Some
Ihh / PTHrP / Sox9 cartilage-growth axis	FLL sources reviewed emphasize bone remodeling, osteoclastogenesis, osteoblastogenesis, mineral metabolism, and oxidative-stress axes. [1-4]	Ihh, PTHrP, and Sox9 are central condylar cartilage regulators for proliferation, differentiation, hypertrophy, and mandibular condylar growth. [6,9]	Overlap is mostly adjacent through downstream ossification and remodeling layers.	Some

Pathway map by biological layer

The same information reorganized from molecular pathway to tissue-level process.

Biological layer	FLL-linked pathways	Condylar / jaw process	Overlap grade
Osteoclast/resorption	RANKL-RANK/TRAF6-NF-kB/MAPK-NFATc1; TRAP; CTSK; MMP-9; OPG/RANKL	Resorption, matrix breakdown, subchondral bone turnover, remodeling response	**Strong**
Osteoblast/ossification	Wnt/beta-catenin; PI3K/Akt; RUNX2; OPN; BMP/Smad	Osteoblast differentiation, mineralization, condylar ossification/remodeling	**Strong / Partial**
Cartilage-growth regulation	Adjacent links through RUNX2, Wnt, BMP/Smad, mineralization, and matrix turnover	Sox9, Ihh, PTHrP, type II collagen, type X collagen, VEGF, chondrocyte maturation	**Some / Partial**
Mineral metabolism	PTH, FGF23, 1,25(OH)2D3, VDR, CaSR, calcium transport	Mineral availability and bone quality during jaw remodeling	**Partial**
Stress/inflammation	Nox4/ROS/NF-kB; Nrf2/HO-1; ferroptosis; oxidative stress	TMJ matrix turnover, inflammatory remodeling, cell survival	**Some / Partial**
Endocrine/systemic	ER-alpha/ER-beta; gut microbiota/TMAO/Sirt6	Hormonal and systemic bone-homeostasis background	**Some**

Selected references

[1] Chen et al. Fructus Ligustri Lucidi in Osteoporosis: A Review of its Pharmacology, Phytochemistry, Pharmacokinetics and Safety. Molecules. 2017;22:1469.
[2] Xu et al. Fructus Ligustri Lucidi ethanol extract inhibits osteoclastogenesis in RAW264.7 cells via the RANKL signaling pathway. Molecular Medicine Reports. 2016;14:4767-4774.
[3] Kong et al. The potential mechanism of Fructus Ligustri Lucidi promoting osteogenetic differentiation of BMSCs based on network pharmacology, molecular docking and experimental identification. Bioengineered. 2022;13:10640-10653.
[4] FLL osteoporosis studies summarized in FLL pharmacology and bone-quality literature, including canonical Wnt/beta-catenin signaling.
[5] Kapoor et al. Biomolecular signals in mandibular condylar cartilage: Bioinformatics and evidence-based insights for optimizing functional appliance therapy. Seminars in Orthodontics. 2025.
[6] Yang and Ren. Factors Involved in Mandibular Condylar Growth: An Overview. Oral Health and Dental Management. 2014;13:1019-1023.
[7] Yang et al. Mechanoresponsive and lubricating changes of mandibular condylar cartilage associated with mandibular lateral shift and recovery in the growing rat. Clinical Oral Investigations. 2020;24:3547-3557.
[8] Osteoblast-osteoclast communication and OPG/RANKL/cathepsin K pathways reported in FLL bone-remodeling studies.
[9] PTHrP/Ihh/Sox9 condylar growth axis described in mandibular condylar cartilage growth and MCC development literature.
[10] Ligustri Lucidi Fructus postmenopausal osteoporosis studies identifying BMP-Smad/Runx2-related mechanisms.
[11] FLL bone studies reporting Nrf2/HO-1 and ferroptosis-related osteoporosis mechanisms.
[12] FLL bone-quality studies reporting gut microbiota diversity, oxidative stress, TMAO, and Sirt6-related effects.