Supplementary table 1. Selection of genetic diseases affecting bone and brain

	disorder	disorder	effect on brain and bone	studies/reviews
brain and bone	*genetic*	hereditary inclusion body myopathy (IBMPFD)	- associated with paget disease of bone (PDB) and frontotemporal dementia (FTD) is a progressive autosomal dominant that manifests as one or both diseases associated, caused by valosin-containing protein (VCP) mutations - **brain**: 31% of patients develop FTD characterized with antisocial behavior, language dysfunction up to cortical degenerative changes - **bone**: 51% of patients show osteolytic lesions with increased and disorganized bone remodeling consistent with PDB	[38] [39] [40]
		Lenz-Majewski syndrom (LMS)	- heterozygous mutations in the *PTDSS1* gene encoding PSS1, one of the two enzymes involved in the production of phosphatidylserine - **brain**: intellectual disability - **bone**: progressive generalized craniotubular hyperostosis with distinct craniofacial, dental, cutaneous and limb anomalies	[41]
		Nasu-Hakola Disease (NHD or PLOSL)	- also called polycystic lipomembranous osteodysplasia with sclerosing leuko-encephalopathy (PLOSL), caused by *TYROBP* (*DAP12*) and *TREM2* mutations - **brain**: associated with a special form of neurodegeneration that leads to dementia (approx. 4th decade of life) and death (approx. 5th decade of life) - **bone**: characterized by multiple bone cysts leading to Fx	[42]
		tricho-rhino-phalangeal syndrome (TRPS)	- autosomal dominant deletion on chromosome 8, TRPS I (pathogenic variant of *TRPS1*) and TRPS II (deletion of *TRPS1*, *RAD21* and *EXT1*) - **brain**: intellectual disability is uncommon in TRPS I, but in most cases of TRPS II with typically mild to moderate in severity - **bone**: both types characterized by distinctive facial features, short stature and skeletal anomalies, only TRPS II with multiple osteochondromas	[43]

Supplementary table 2. Selection of genetic polymorphism affecting brain and bone

	gene	effect of genetic polymorphism on brain and/or bone	studies/reviews
brain	*CARTPT*	- affects lumbal spine bone mineral density (BMD)	[10]
	VIP	- predicts treatment requirement in early rheumatoid arthritis	[7]
	POMC	- associated with low BMD; haplotypes could be useful markers for predicting antidepressant treatment in major depressive disorder (MDD) patients	[8,9]
	NPY	- polymorphism in neuropeptide Y (NPY) and NPY receptor genes may be useful in identifying women at risk for osteoporosis	[10]
bone	*BGLAP*	- may effect the risk of osteoporosis and fracture in a gender dependent manner	[1,2]
	SOST	- associated with BMD, sclerosteosis and van Buchem disease while increased promotor methylation promotes bone formation and may be related to severity of osteogenesis imperfecta	[3-6,44-46] [16,47]
	LRP5	- activating mutations leads to high bone mass while inactivating mutations result in osteoporosis	[48,49]
brain and bone	*DKK1*	- multifaceted effects on proliferation and differentiation of various human cells such as osteoblasts and bone marrow cells	[16]
	TNFSF11	- associated with BMD and high risk for Paget's disease	[17-21]
	BDNF	- Val66Met polymorphism presence is a risk factor for psychosis in neurodegenerative diseases such as Alzheimer's and Parkinson's disease	[22-24]
	IGF-1	- significantly associated with BMD and osteoporosis in postmenopausal woman, suggesting rs35767 as predictive factor for osteoporosis risk	[25-29]
	BMP2	- controversy results show different BMD alterations; associated with ossification of the posterior longitudinal ligament	[30-34]
	BMP4	- polymorphism contributes to risk of non-syndromic cleft lip with or without cleft palate and influences early marginal bone loss around implants	[35,36]
	BMP7	- associated with inverse relationships between bone mineralization and vascular calcification	[37]

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