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Ultrashort Peptides Induce Biomineralization

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Ultrashort peptides induce biomineralization

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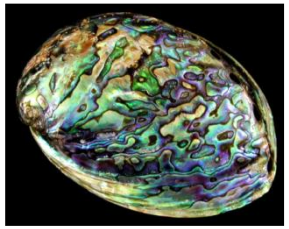
Principal components of biomineralized materials

Calcium phosphate (hydroxyapatite $Ca_5(PO_4)_3OH$) + collagen

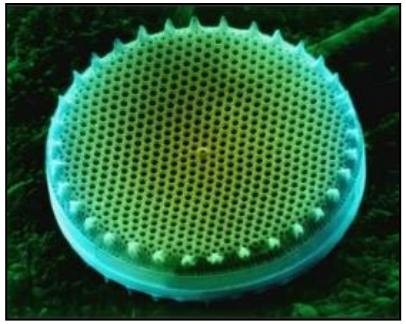





Calcium carbonate ($CaCO_3$) + chitin + protein



Amorphous Silica $SiO_2 \cdot nH_2O$

Meyers MA, et al. 2008

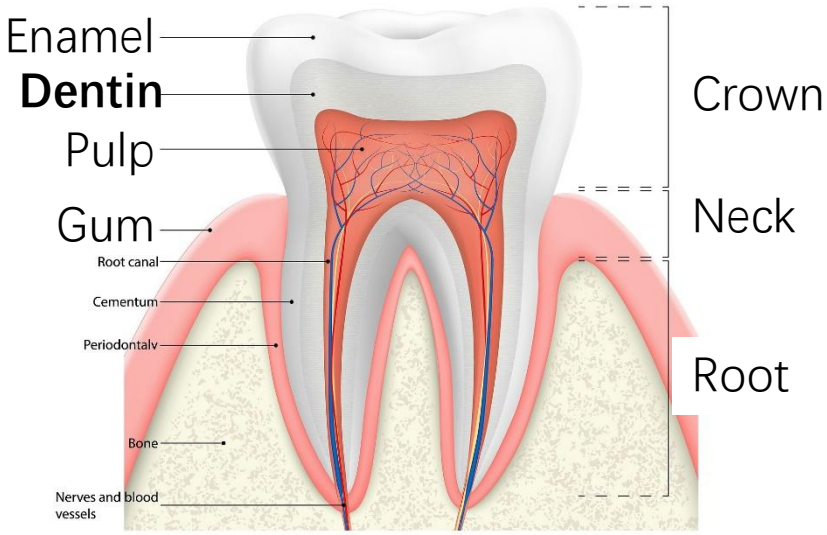
Minerals in Biological System

	Chemical formula	Distribution
Barium sulfate	$BaSO_4$	Algae (gravity sensor)
Calcium carbonate	$CaCO_3$	
Calcite (rhombohedral)		Mollusk shells, bird eggs, sponge spicules, sea urchin spines
Aragonite (orthorhombic)		Mollusk shells, corals
Amorphous		Arthopod exoskeletons, mollusk shells, plants
Calcium oxalate	CaC_2O_4	Kidney stones, plants
Calcium sulfate	$CaSO_4$	Jellyfish larvae (gravity sensor)
Dolomite	$CaMg(CO_3)_2$	Sea urchin spicules and teeth
Ferrihydrate	$5Fe_2O_3{\cdot}9H_2O$	Ferritin (animals), plants
Greigite	Fe_3S_4	*Crysomallon squamiferum* foot (gastropod living near hot vents in Indian Ocean)
Hydroxyapatite (HA)	**$Ca_5(PO_4)_3(OH)$**	**Bones, teeth, osteoderms**
Iron(III)oxide/hydroxide	FeOOH	Chitin and limpet teeth
Magnetite	Fe_3O_4	Mollusk radula, bacteria
Pyrite	FeS_2	*Crysomallon squamiferum* foot (gastropod living near hot vents in Indian Ocean)
Silica (hydrated)	$SiO_2{\cdot}nH_2O$	Diatom exoskeleton, sponge spicules

Compositions of bones and teeth

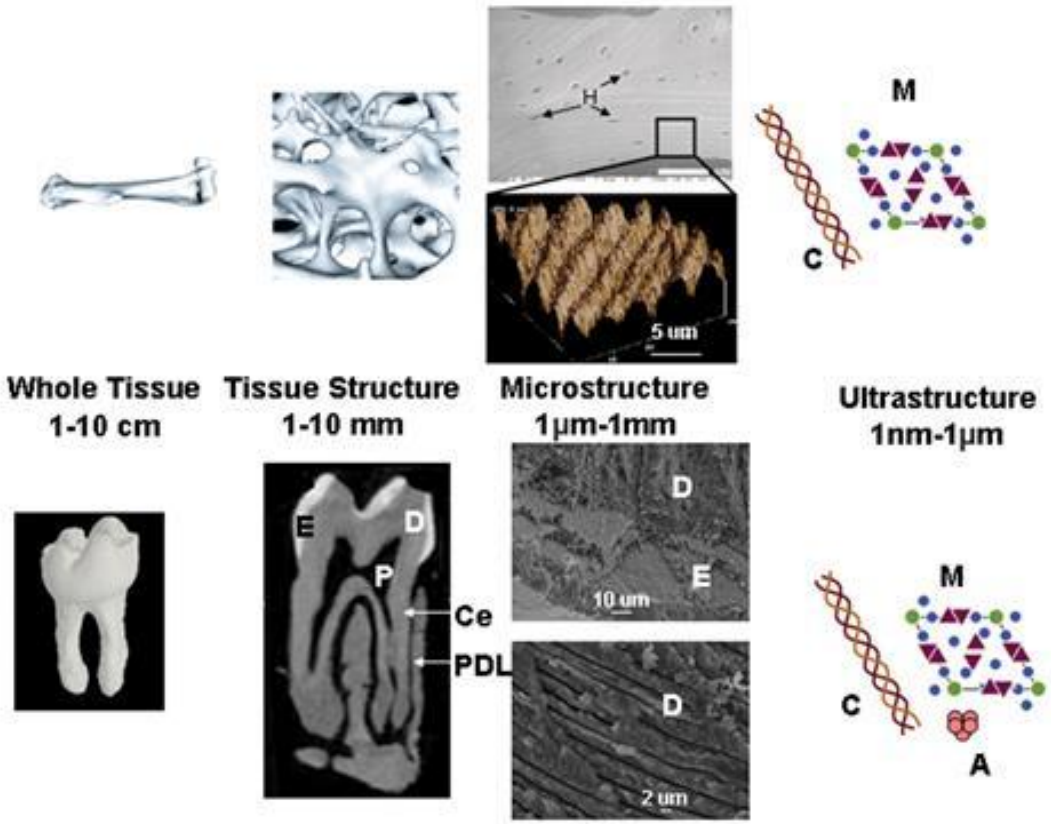
Composed of mineralized **calcium phosphate** (specifically, the calcium phosphate phase called hydroxyapatite (HA) $Ca_5(PO_4)_3OH$) within a matrix of **collagen fibrils** (~1/3 dry weight, 50% of bone by volume, **90% of protein content**) and **200 other proteins** (e.g., acidic glycoproteins, proteoglycans & carboxylated proteins comprising the other **10% by weight**)

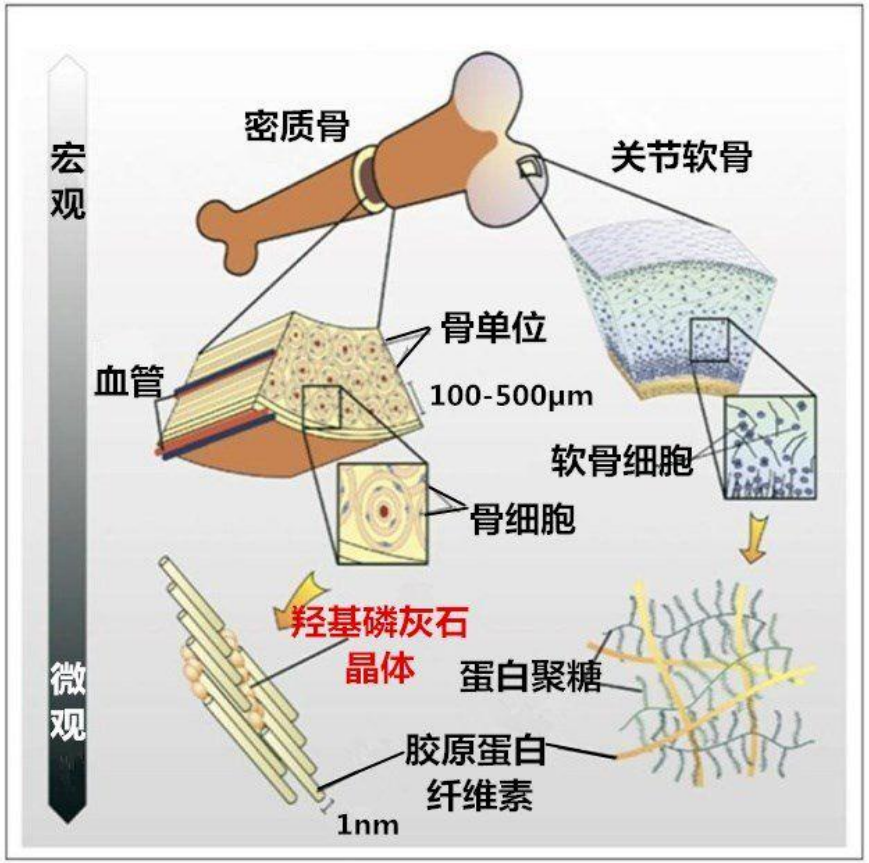
HA is a '**living mineral**' that is continually grown, dissolved & remodeled in response to signals of internal (e.g., pregnancy) and external (e.g., gravity, exercise) origin



Dentin contains collagen and is similar in composition to bone

Biomineralization across length scales

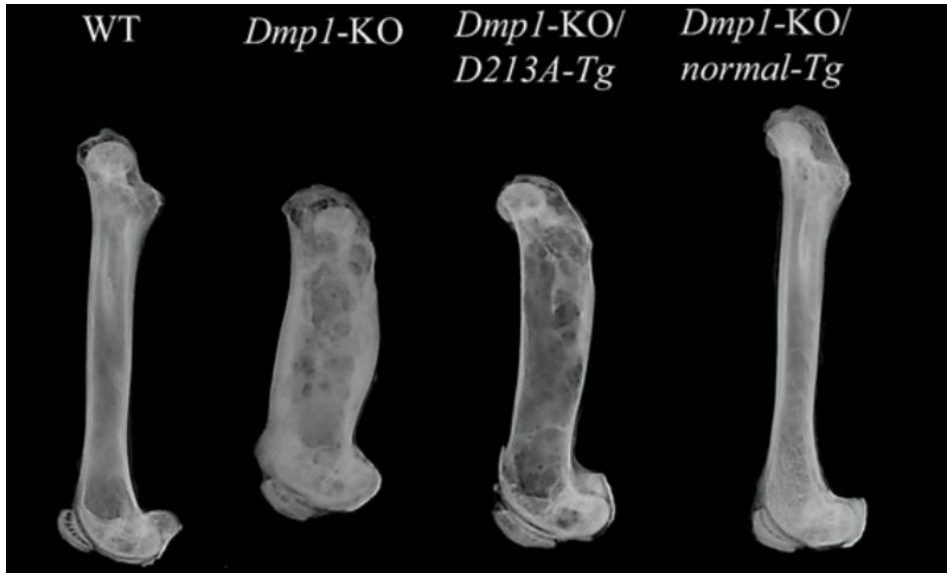




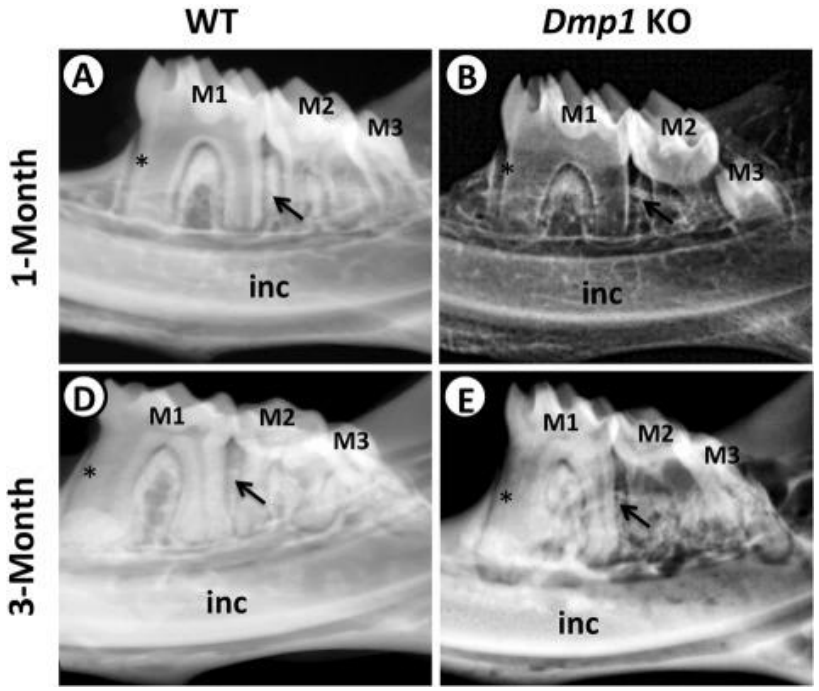
Boskey, AL. *Elements* 2007

Physiological roles of dentin matrix acidic phosphoprotein 1 （DMP1）

KO of DMP1 induces defects in bone and tooth development



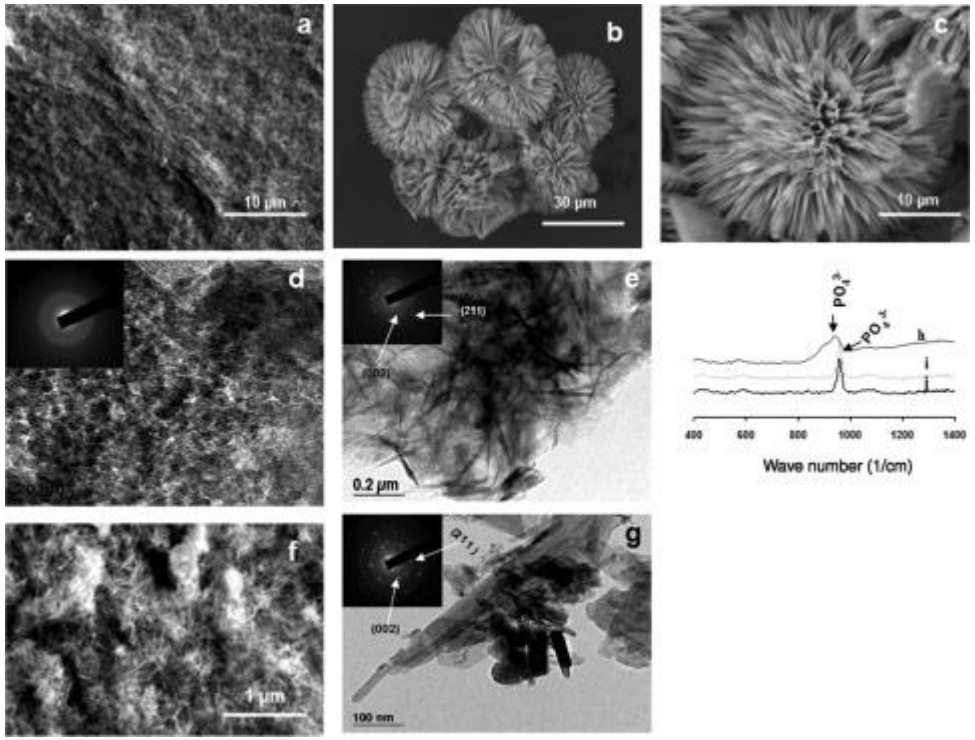
Sun Y, et al. Cells Tissues Organs. 2011



Gibson MP, et al. J Biol Chem. 2013

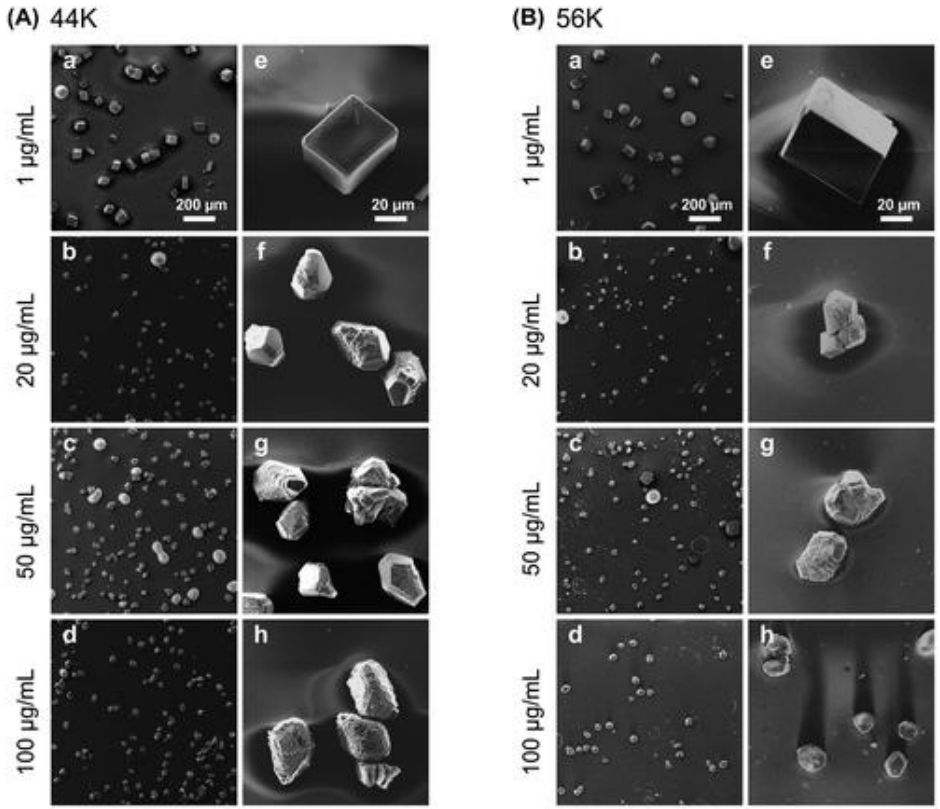
DMP1 regulates biomineralization *in vitro*

$Ca_5(PO_4)_3(OH)$



Gajjeraman S, et al. J Biol Chem. 2007

$CaCO_3$

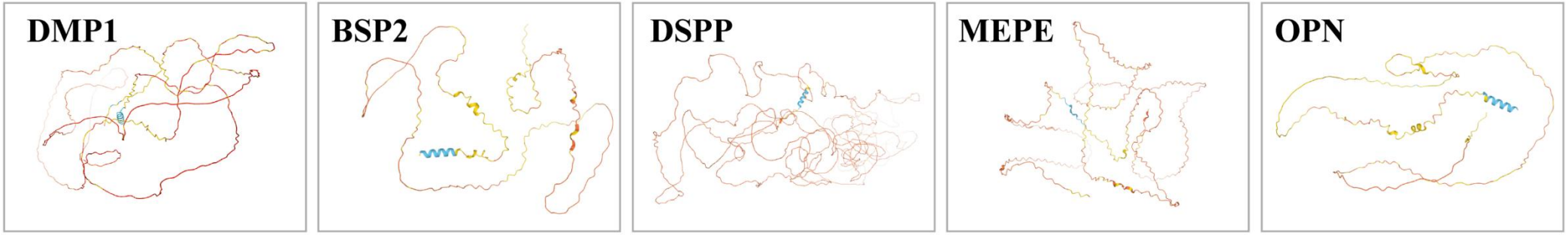


Porębska A, et al. FASEB J. 2020

Peptide derivative of DMP1: SESSE

Small integrin-binding ligand N-linked glycoprotein (SIBLING) family

a



b

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  1 MKISILLMFL WGLSCALPVT RYQNNESEDS EEWKGHLAQA PTPPLESSES SEGSKVSSEE
 61 QANEDPSDST QSEEGLGSDD HQYIYRLAGG FSRSTGKGGD DKDDDEDDSG DDTFGDDDSG
121 PGPKDRQEGG NSRLGSDEDS DDTIQASEES APQGQDSAQD TTSESRELDN EDRVDSKPEG
181 GDSTQESESE EHWVGGGSDG ESSHGDGSEL DDEGMQSDDP ESIRSERGNS RMNSAGMKSK
241 ESGENSEQAN TQDSGGSQLL EHPSRKIFRK SRISEEDDRS ELDDNNTMEE VKSDSTENSN
301 SRDTGLSQPR RDSKGDSQED SKENLSQEES QNVDGPSSES SQEANLSSQE NSSESQEEVV
361 SESRGDNPDP TTSYVEDQED SDSSEEDSSH TLSHSKSESR EEQADSESSE SLNFSEESPE
421 SPEDENSSSQ EGLQSHSSSA ESQSEESHSE EDDSDSQDSS RSKEDSNSTE SKSSSEEDGQ
481 LKNIEIESRK LTVDAYHNKP IGDQDDNDCQ DGY
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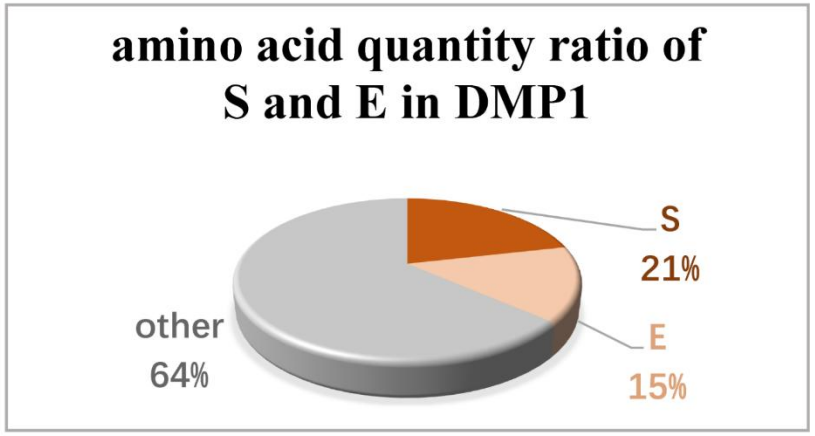
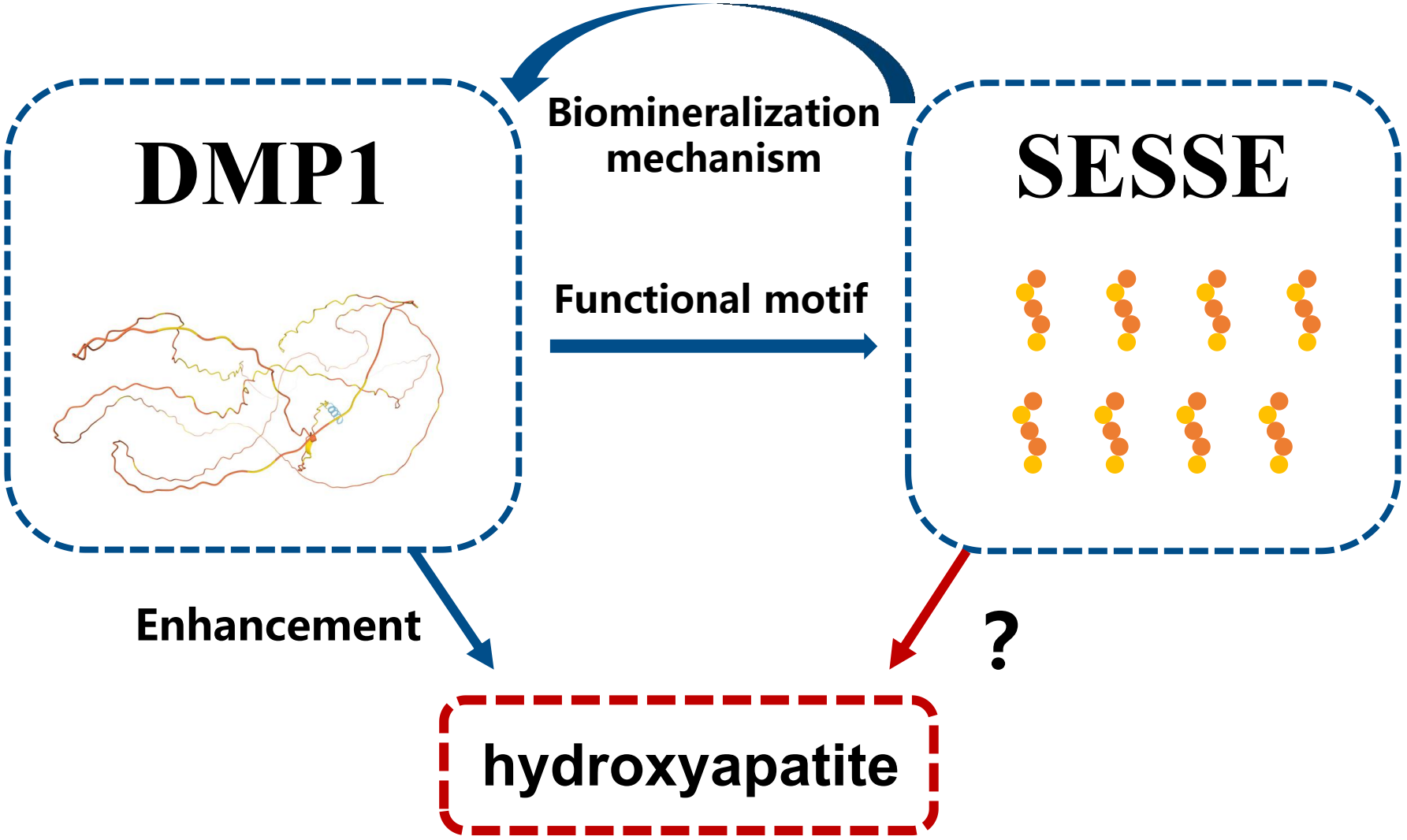
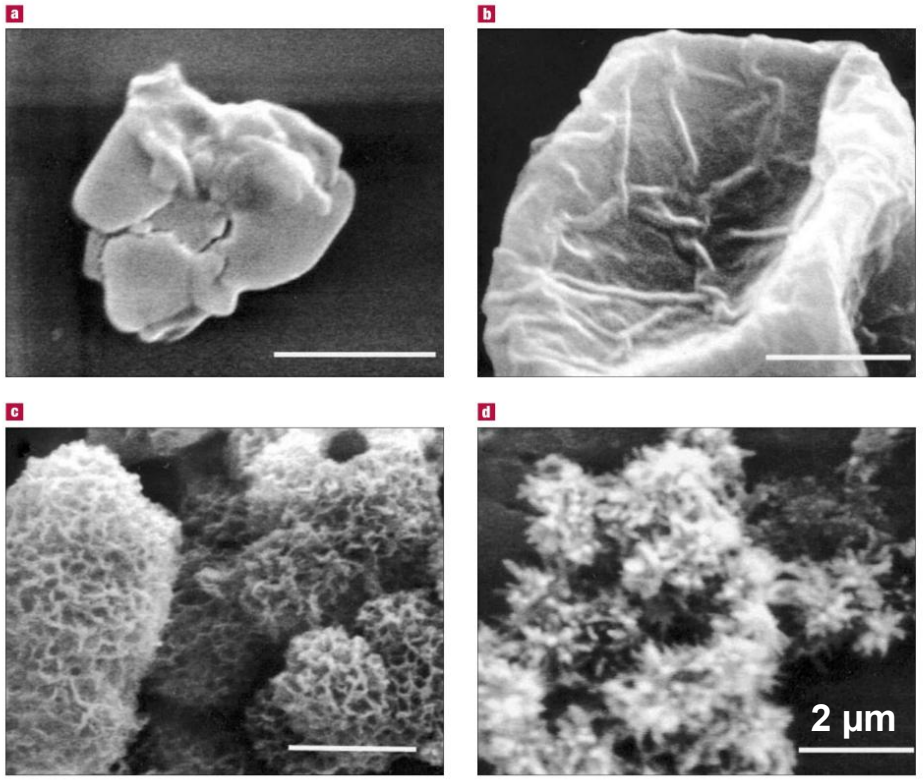


Does the *peptides* induce biomineralization?

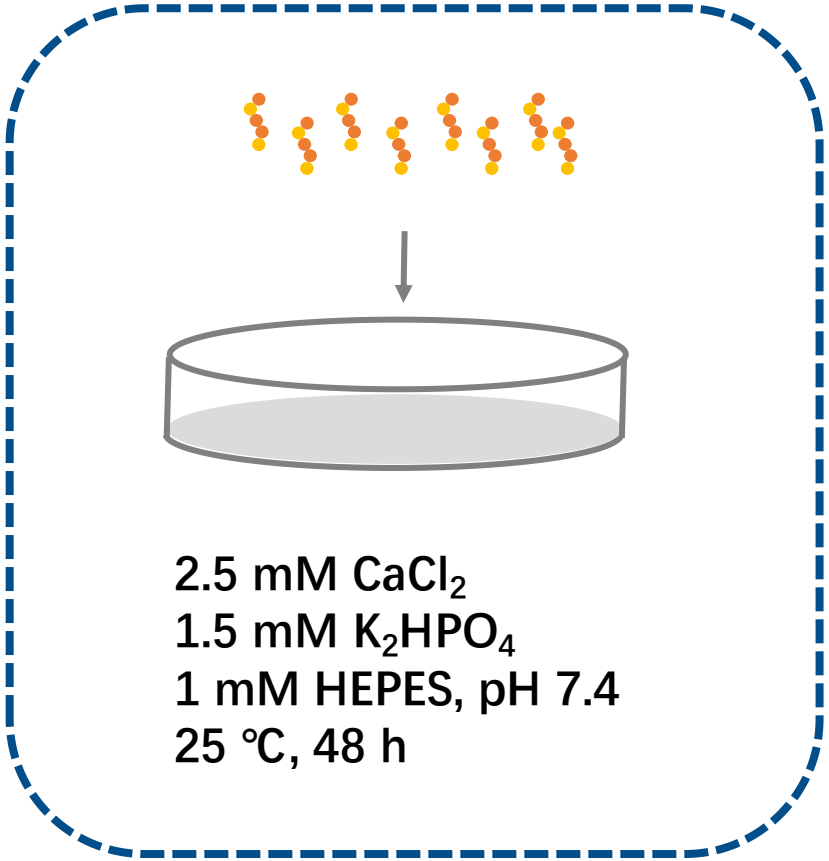


in-vitro system to characterize biomineralization

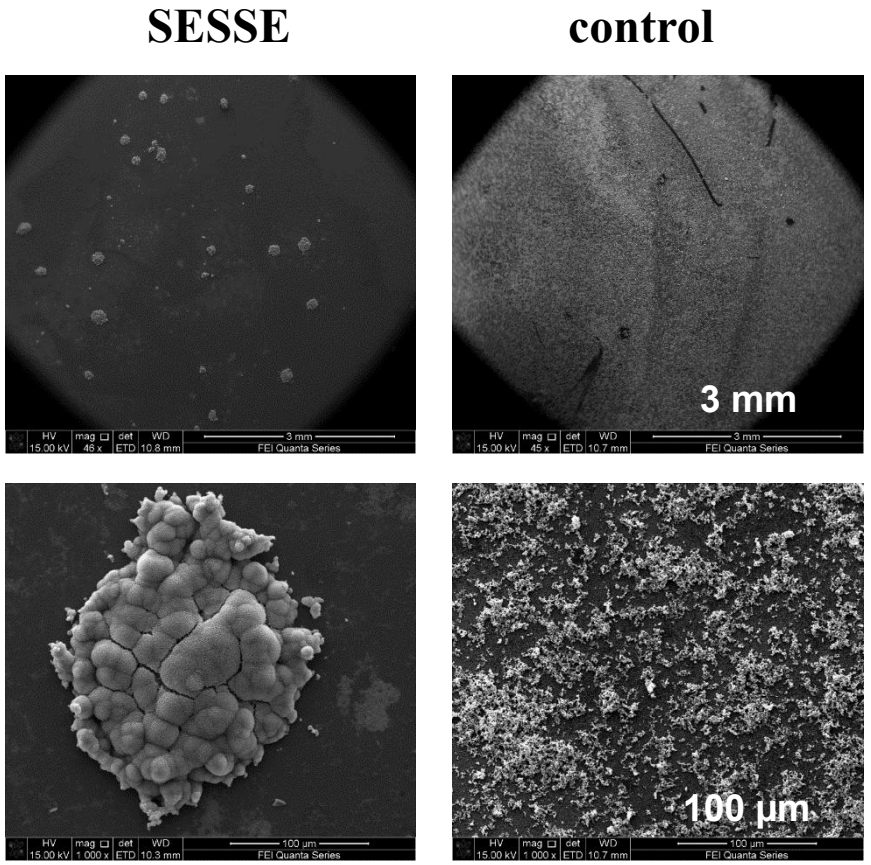
$Ca_5(PO_4)_3(OH)$



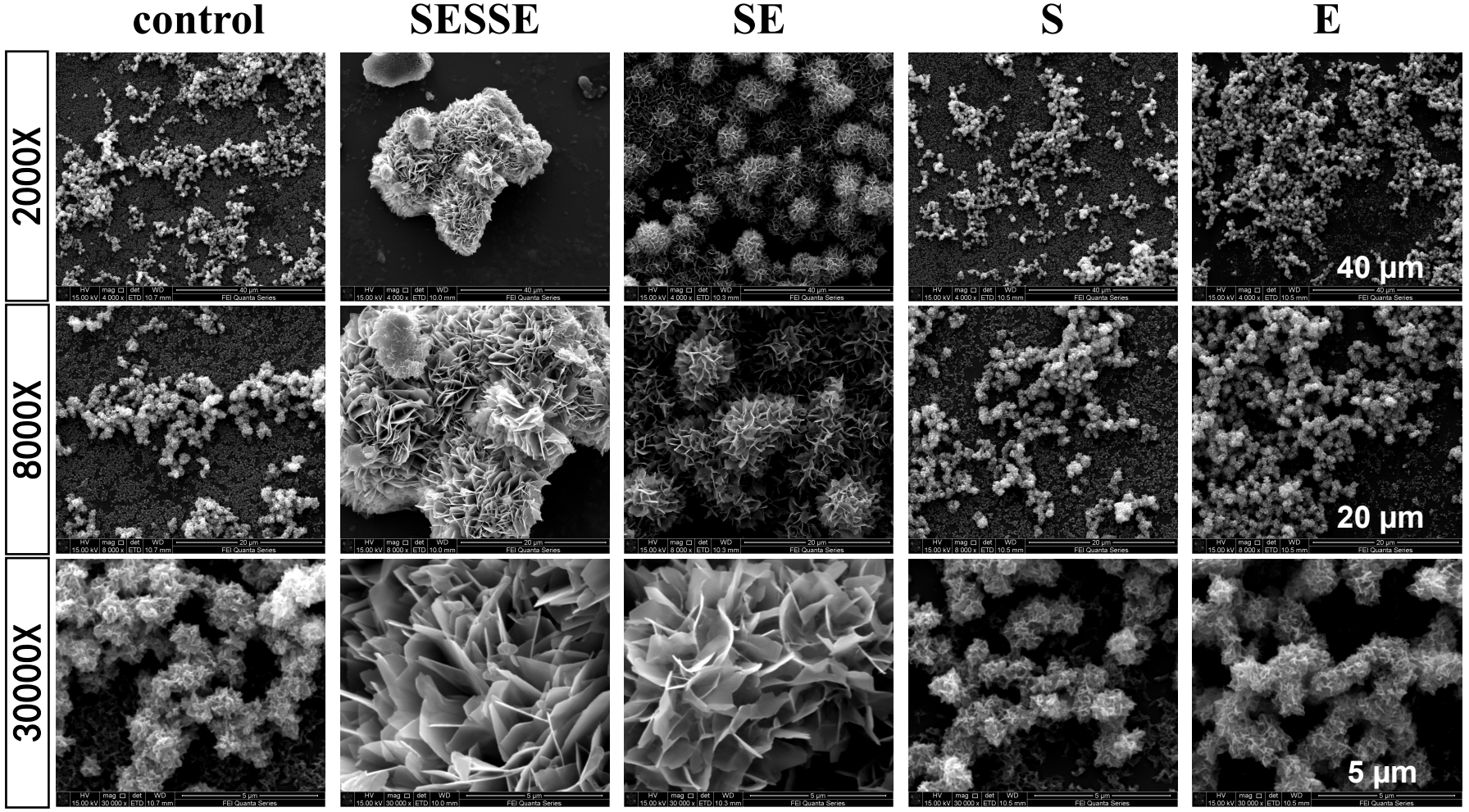
He G, et al. Nature Materials, 2003



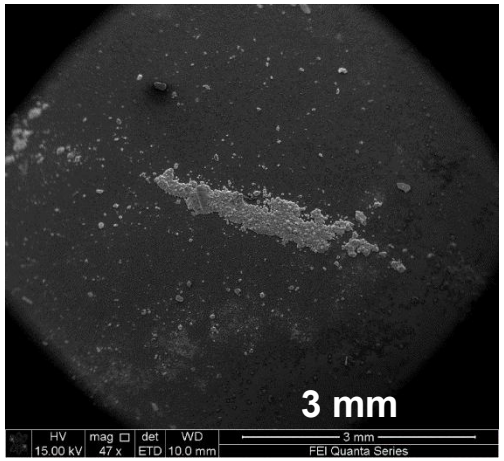
Peptide SESSE induces biomineralization *in vitro*

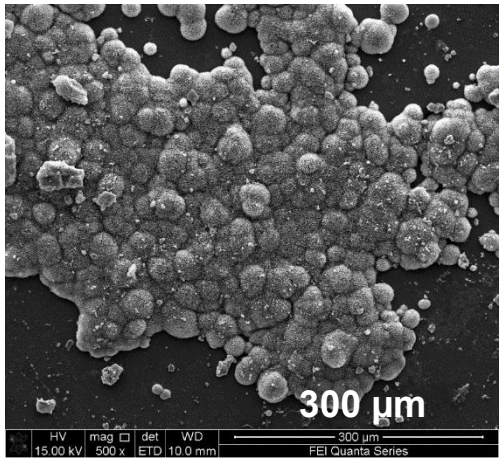


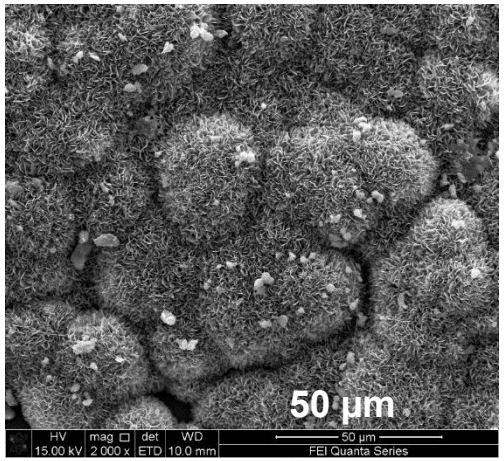
Combinations of S and E induce biomineralization

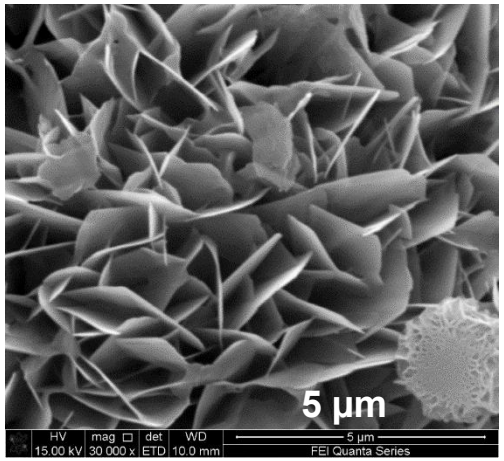


Peptide SESSE induces very large crystal blocks

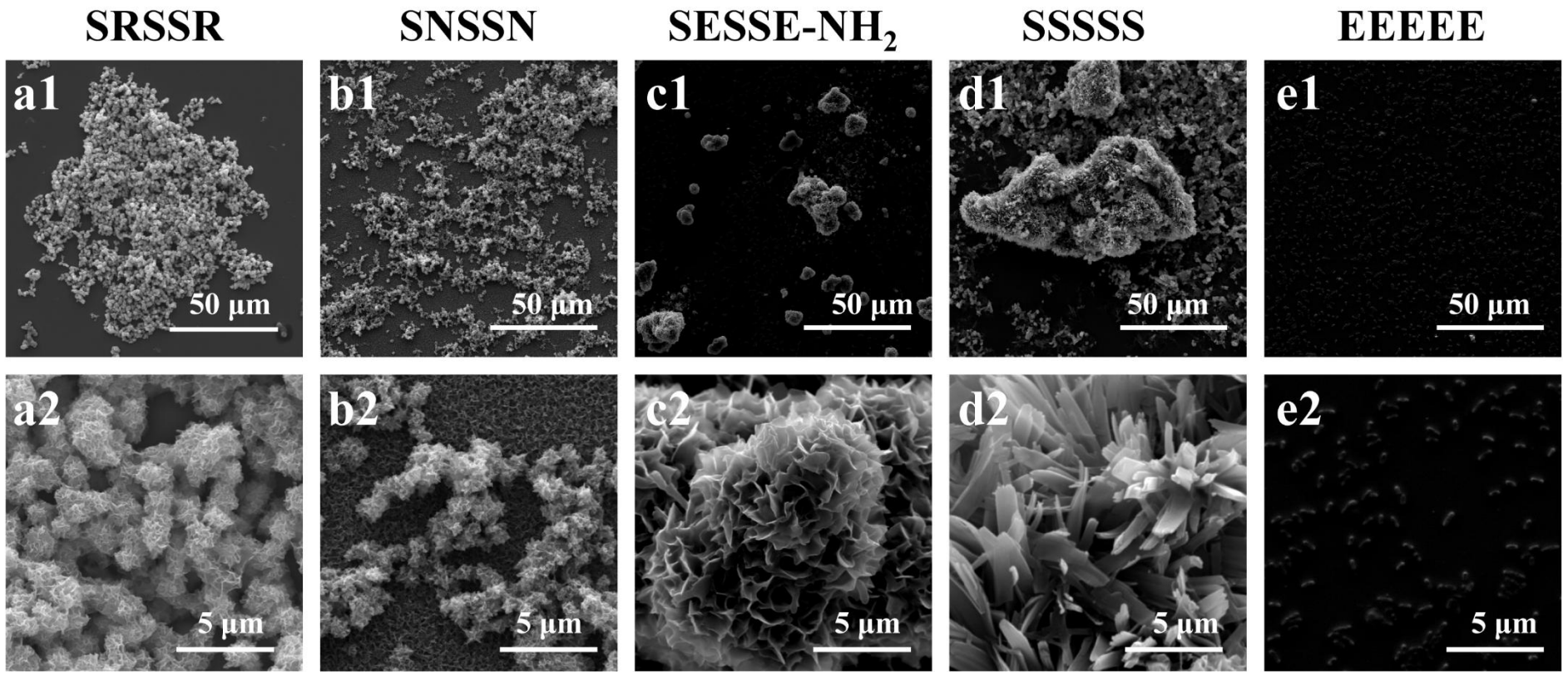




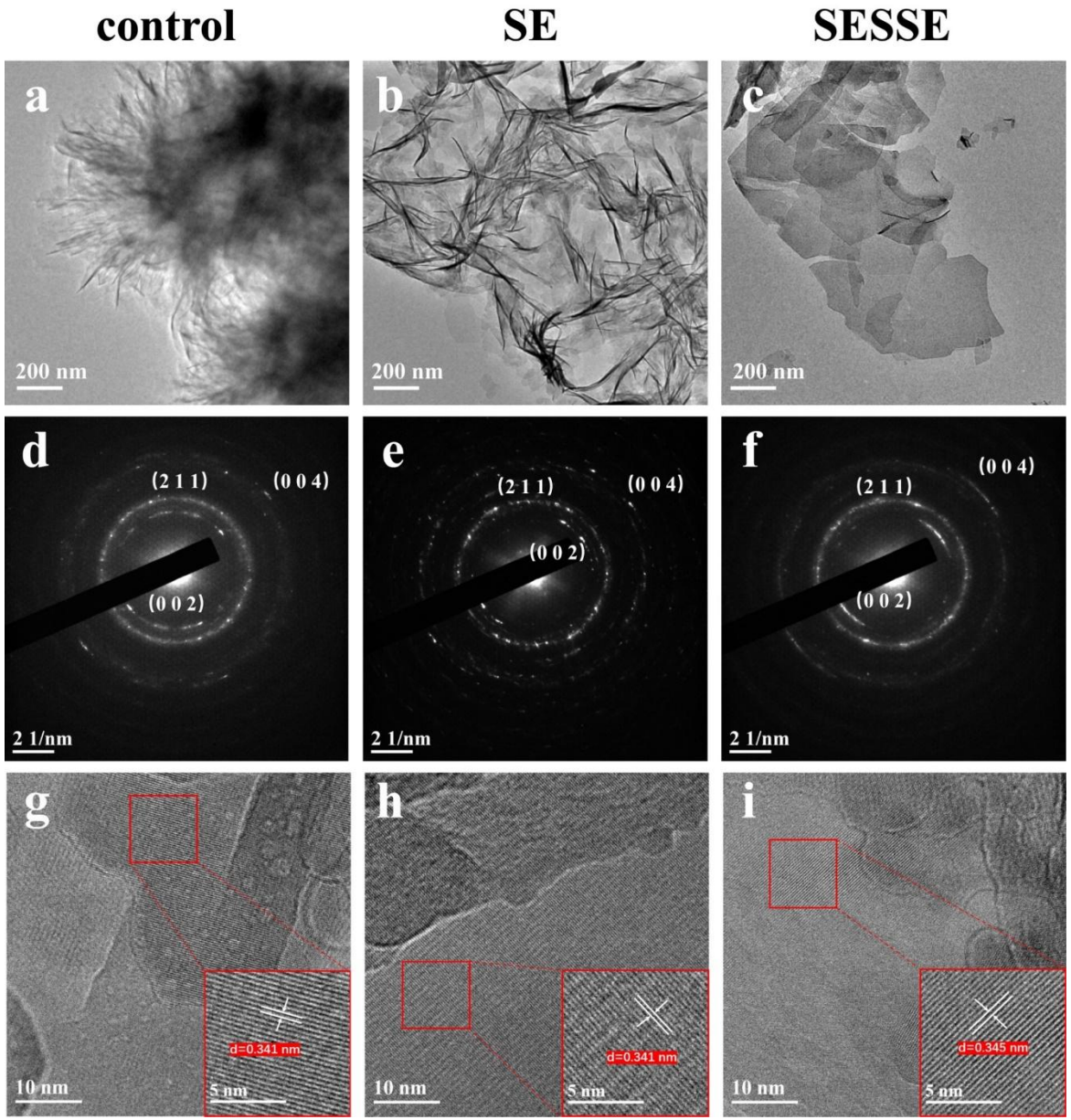




Basic and *neutral polar* peptides fail to enhance crystal formation



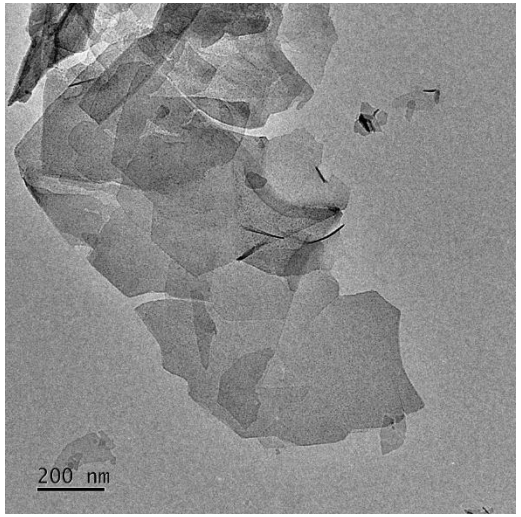
Electron diffraction confirms HA formation

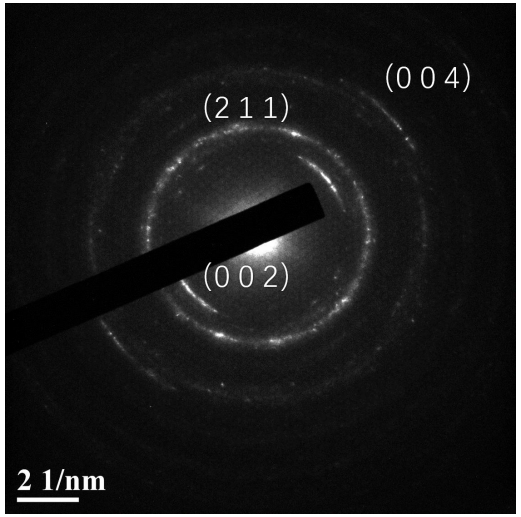


Indexed (0 0 2) (2 1 1) (0 0 4) crystal planes and lattice distance confirm HA formation.

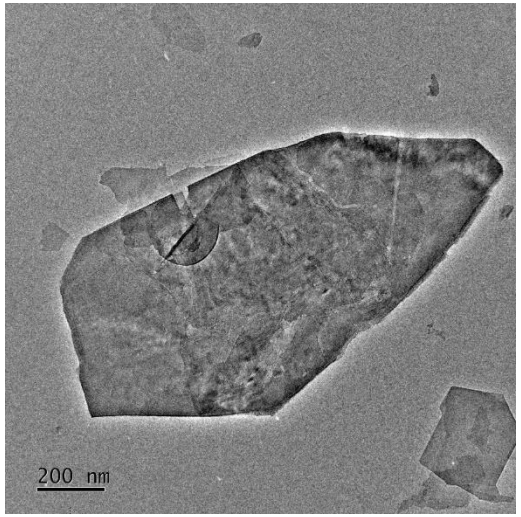
Peptide SESSE has the best capability for biomineralization

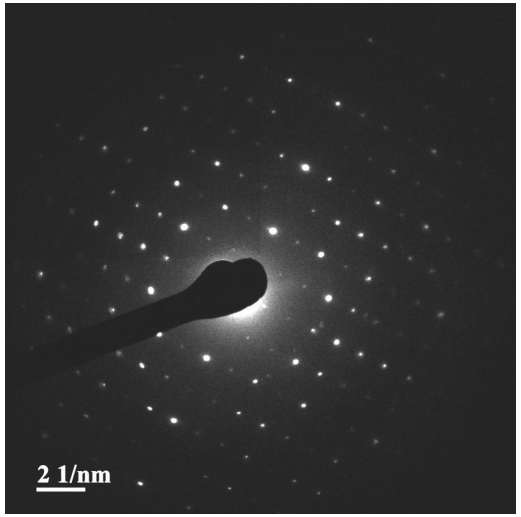
SESSE



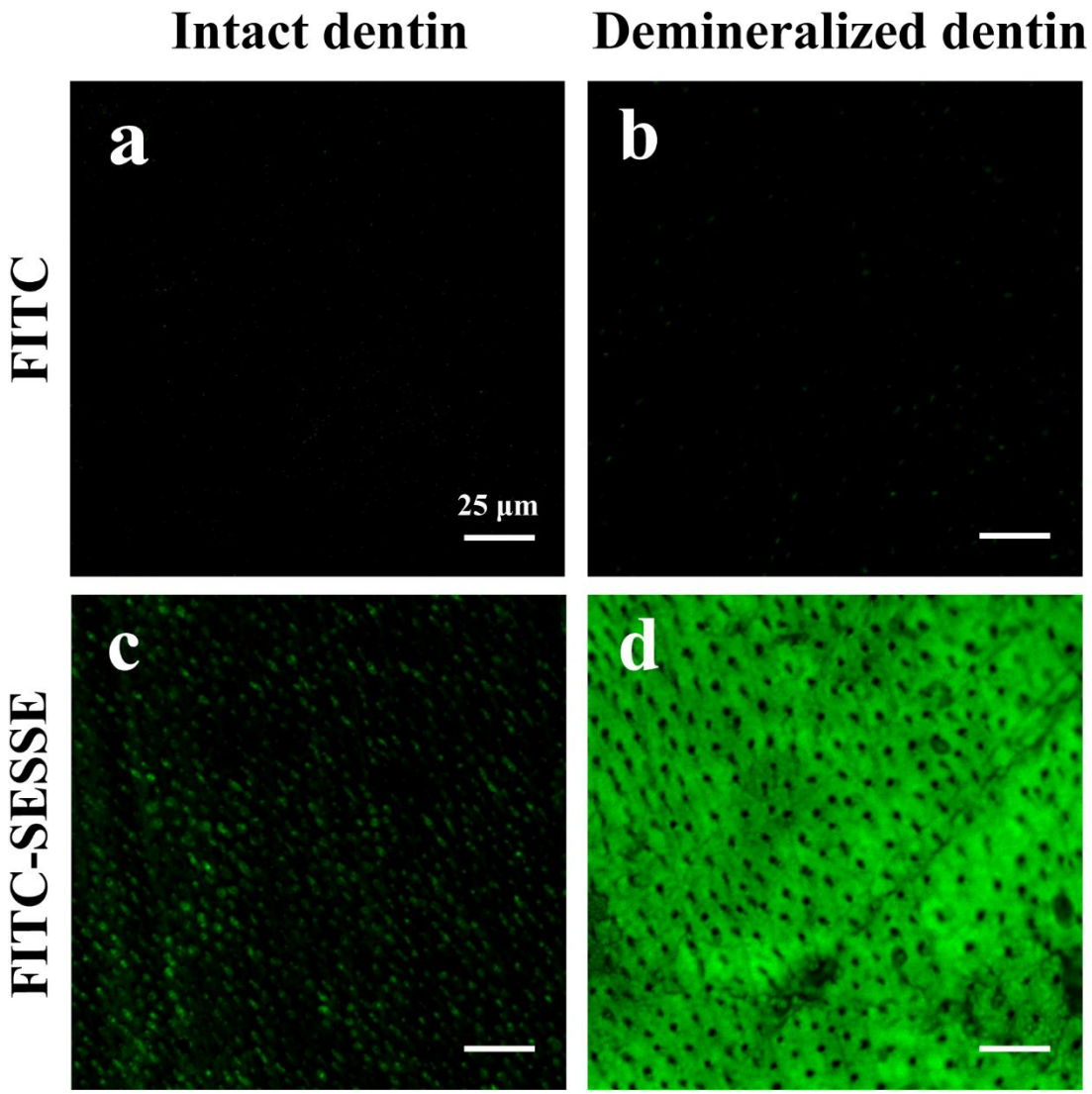


SESSE

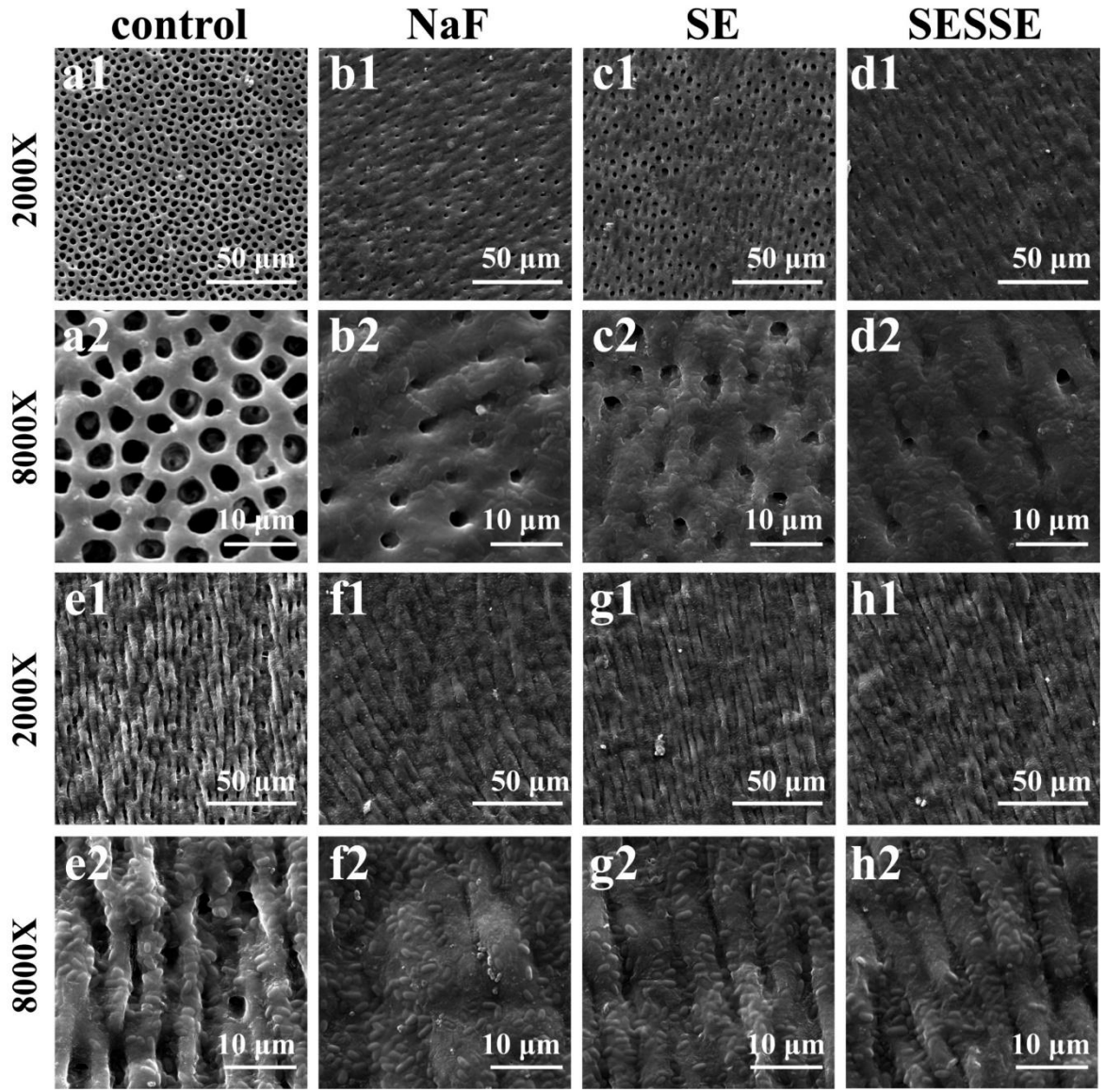




Peptide SESSE has strong affinity for dentins



Peptides SESSE and SE boost dentin remineralization



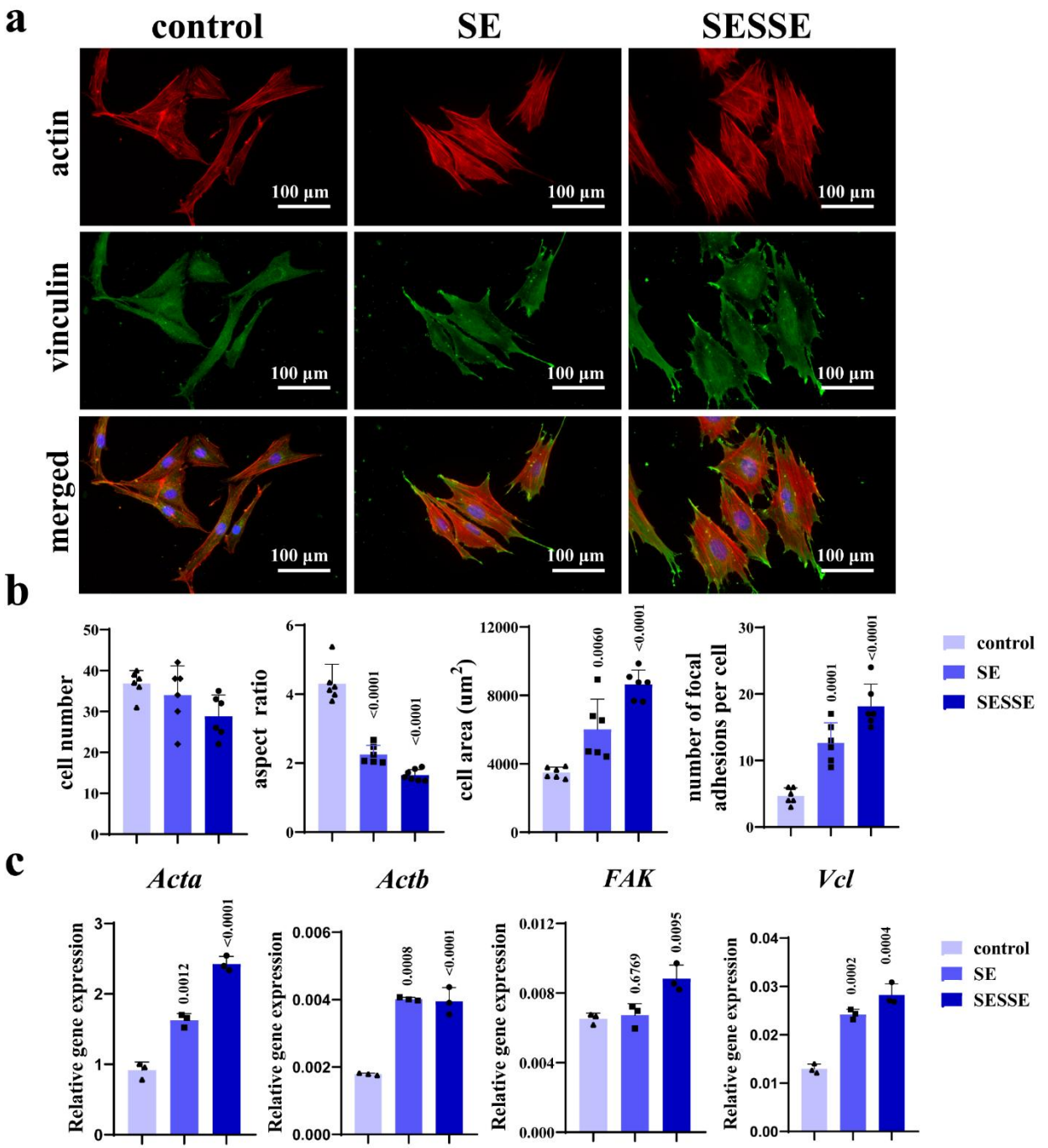
Peptides SESSE and SE promote cell adhesion

ACTA provides instructions for making a protein called α-actin, which is part of the actin protein family

ACTB provides instructions for making a protein called β-actin, which is part of the actin protein family

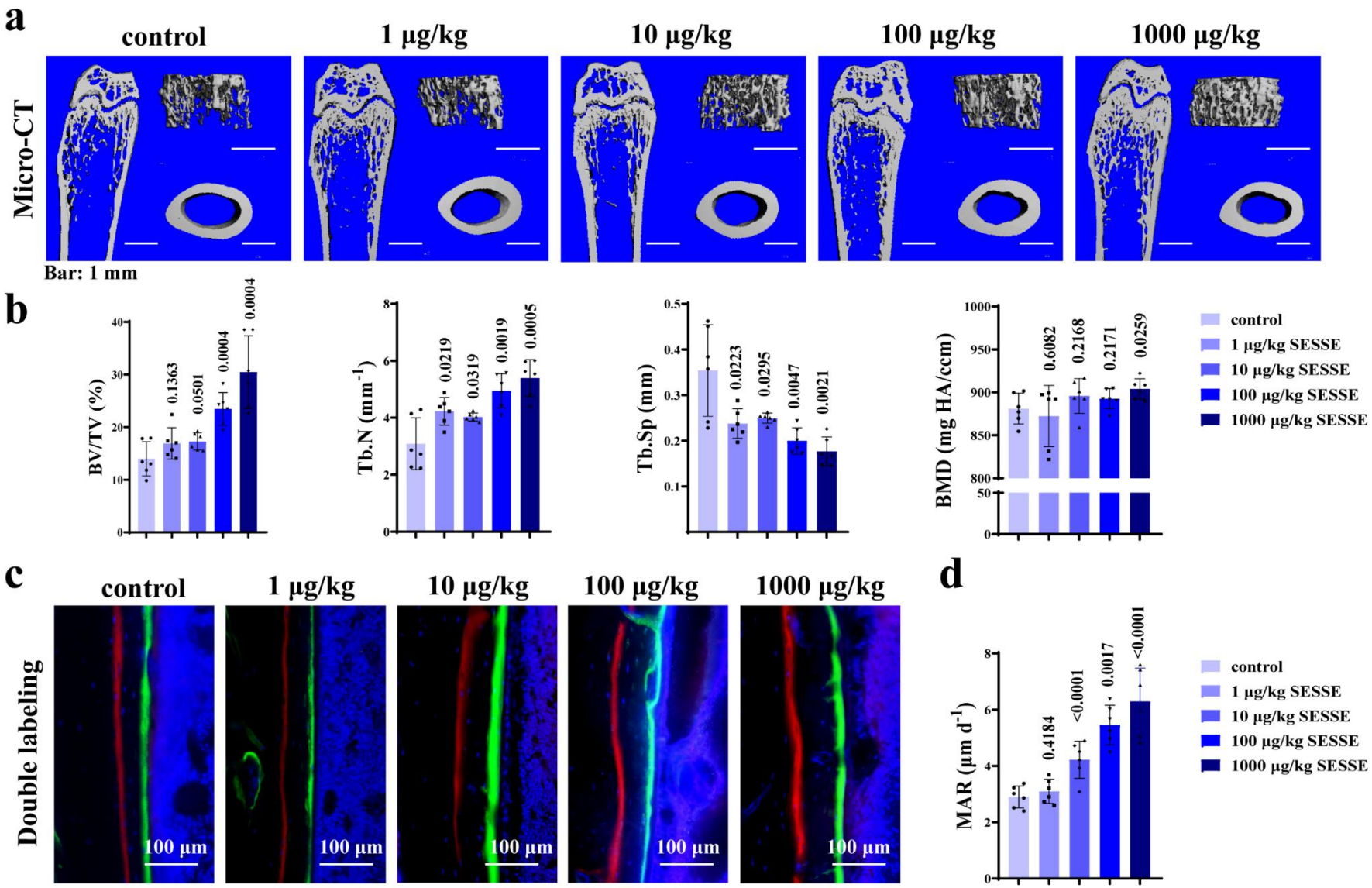
Focal adhesion kinase (**FAK**)

Vinculin (**VCL**) is a cytoskeletal protein associated with cell-cell and cell-matrix junctions

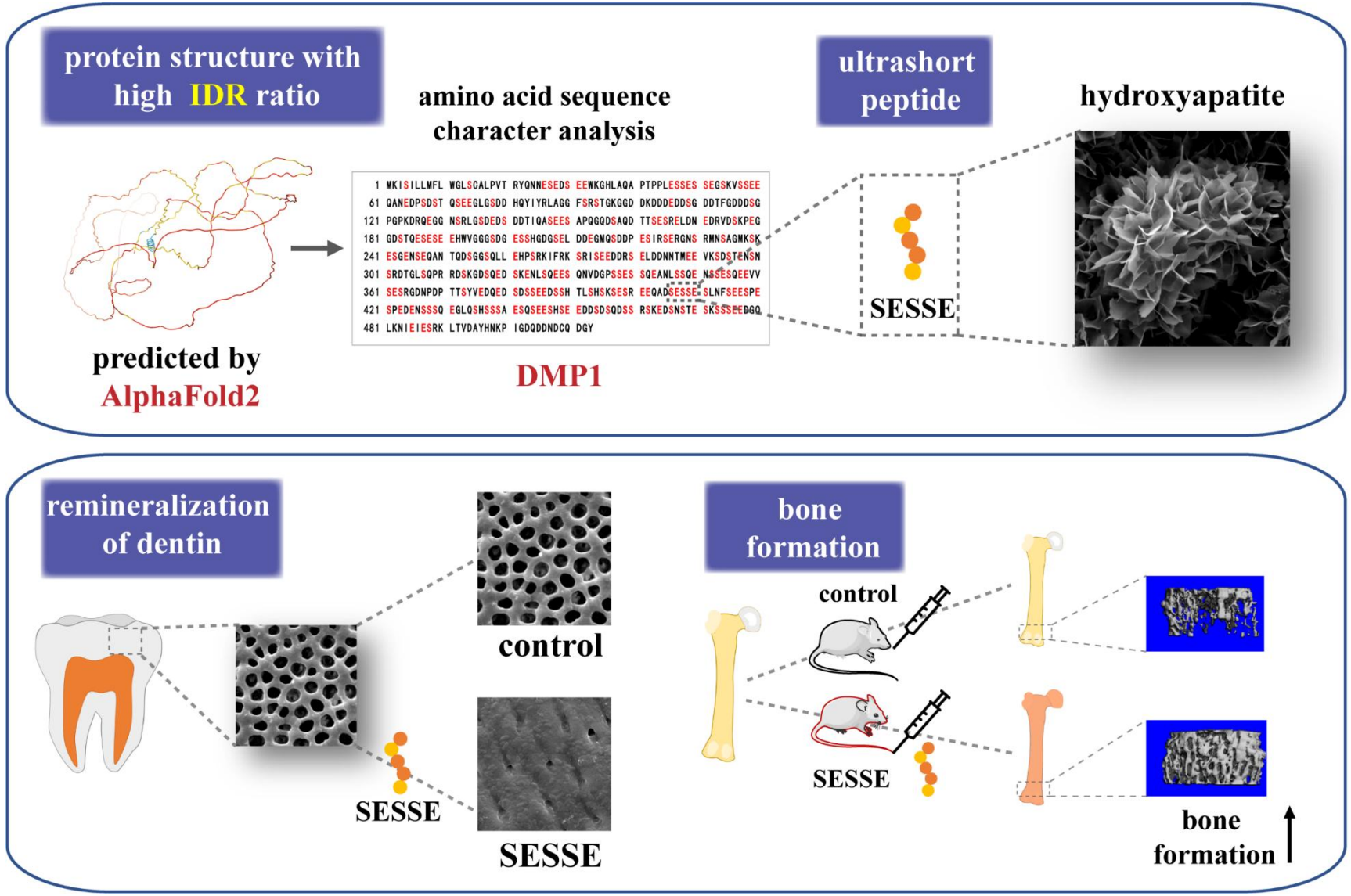


Peptide SESSE improves bone formation *in vivo*

BV/TV:
bone vol./total vol.
Tb.N:
trabecular number
Tb.Sp:
trabecular separation
BMD:
bone mineral density
MAR:
mineral apposition rate



Summary


protein structure with high IDR ratio
predicted by AlphaFold2
amino acid sequence character analysis
1 MKISILLMFL WGLSCALPVT RYQNNESEDS EEWKGHLAQA PTPPLESSES SEGSKVSSEE
61 QANEDPSDST QSEEGLGSDD HQYIYRLAGG FSRSTGKGGD DKDDDEDDSG DDTFGDDDSG
121 PGPKDRQEGG NSRLGSDEDS DDTIQASEES APQGQDSAQD TTSESRELDN EDRVDSKPEG
181 GDSTQESESE EHWVGGGSDG ESSHGDGSEL DDEGMQSDDP ESIRSERGNS RMNSAGMKSK
241 ESQENSEQAN TQDSGGSQLL EHPSRKIFRK SRISEEDDRS ELDDNNTMEE VKSDSTENSN
301 SRDTGLSQPR RDSKGDSQED SKENLSQEES QNVDGPSSES SQEANLSSQE NSSESQEEVV
361 SESRGDNPDP TTSYVEDQED SDSSEEDSSH TLSHSKSESR EEQADSESSE SLNFSEESPE
421 SPEDENSSSQ EGLQSHSSSA ESQSEESHSE EDDSDSQDSS RSKEDSNSTE SKSSSEEDGQ
481 LKNIEIESRK LTVDAYHNKP IGDQDDNDCQ DGY
DMP1
ultrashort peptide
SESSE
hydroxyapatite
remineralization of dentin
control
SESSE
SESSE
bone formation
control
SESSE
bone formation