

Bioactive peptides. Formulations and indications

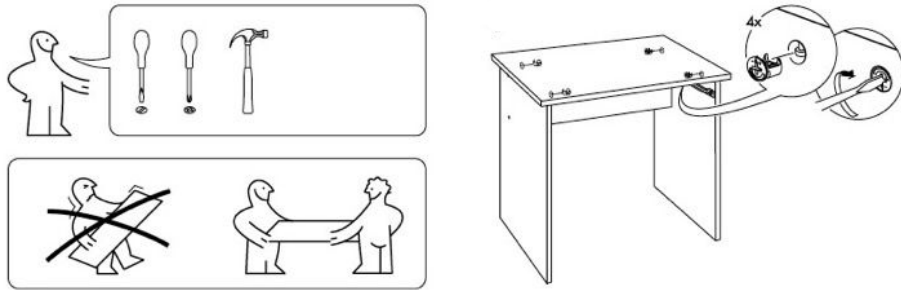
Rick Visser
University of Malaga



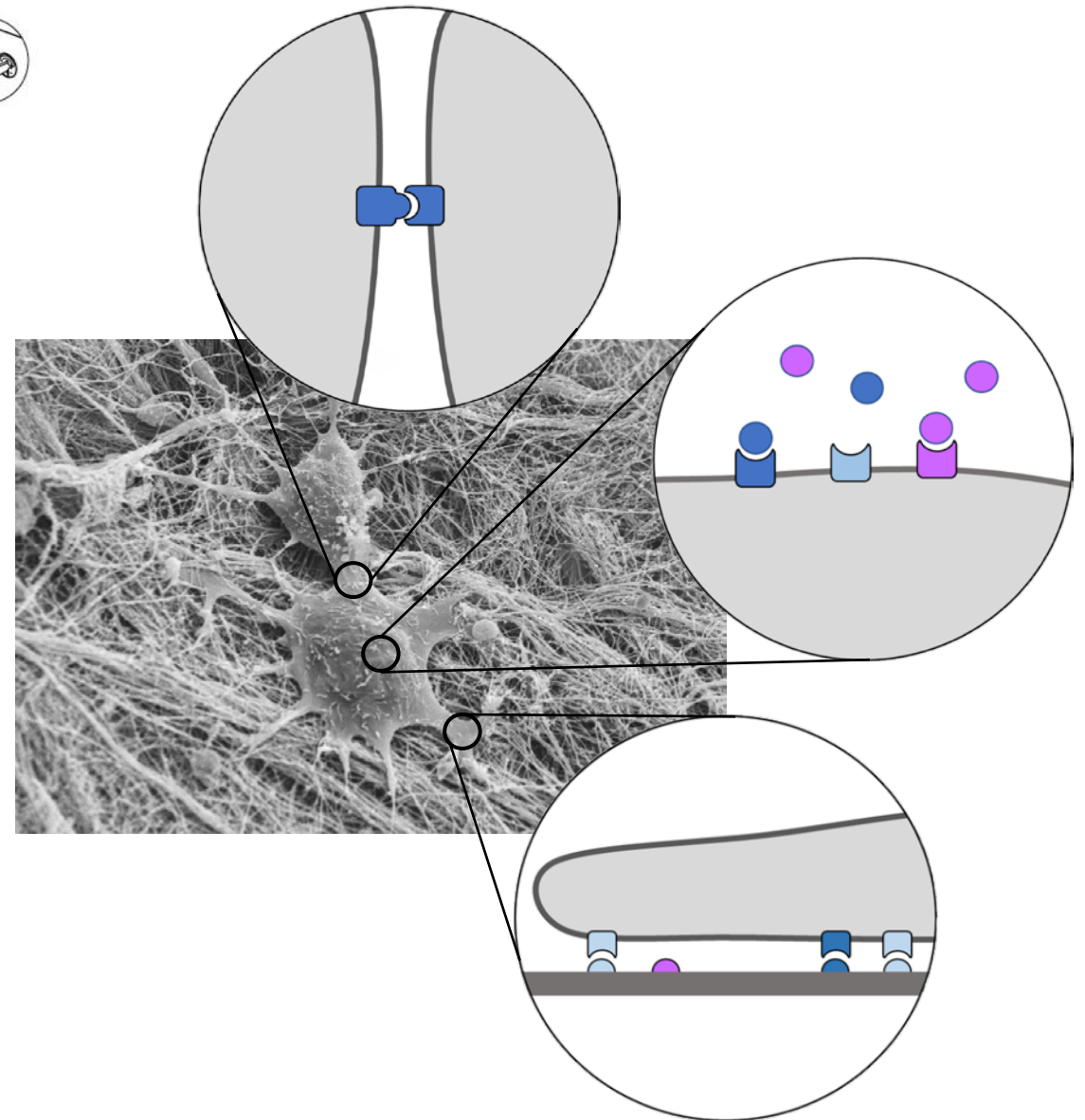
Maastricht, 2022



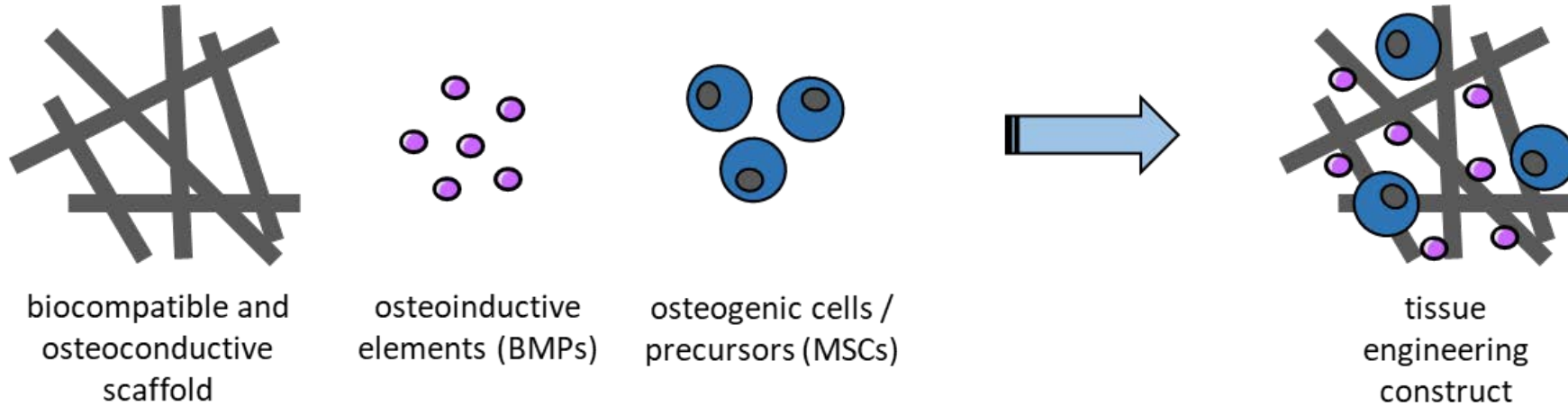
Cells need instructions



Most cells are blind & deaf...
...but they can feel and smell



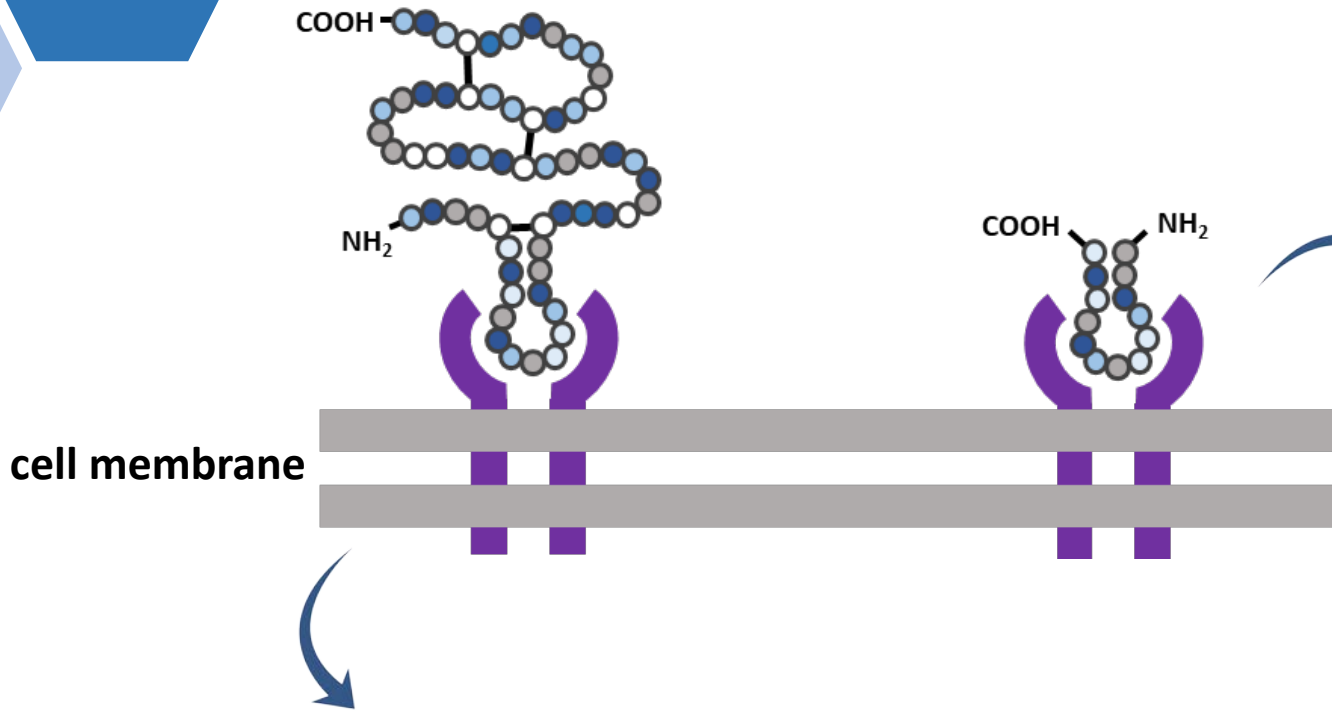
Cells need instructions, also in (Bone) Tissue Engineering



The added bioactive elements (& the biomaterial) should provide instructions for the cells:

- Come here!
- Stay here!
- Attach to this!
- Multiply!
- Form bone, or cartilage, or blood vessels!

Many instructions are encoded in large, complex proteins



cell membrane



- **High activity**
- Well characterized
- Commercially available



- Sensitive
- Expensive
- Immunogenic
- Binding sites for other receptors/cells. Pleiotropy



- More stable
- Cheaper
- Less immunogenic
- Specific
- Smaller size allows for higher densities
- Smaller size allows for easier encapsulation



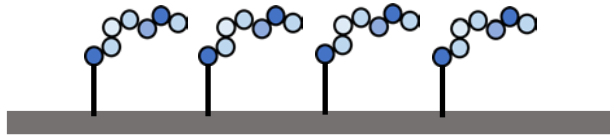
- **Lower activity**
- Poorly characterized
- Many not commercially available

Are peptides always better?

Definitely, not! (but sometimes they can be)

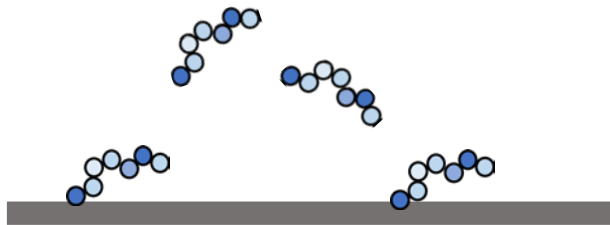
What to consider when approaching a (B)TE strategy involving peptides...

How will the peptide act/interact with its receptors?

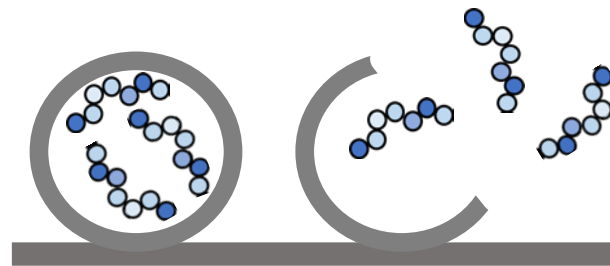


Does it need anchorage to a surface?

Does it need a specific density or spatial distribution?



Does it need to be released?



Does it need a delayed or triggered release?

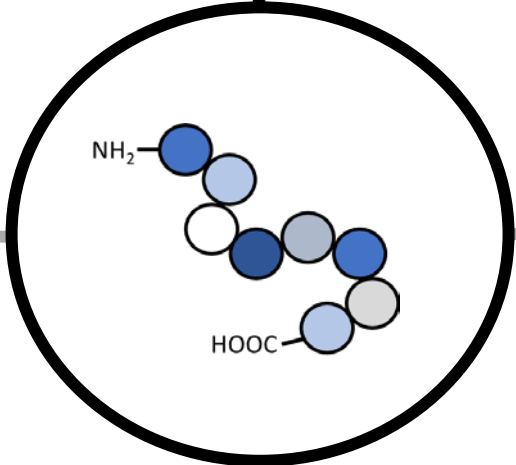
Peptide name	Sequence	Source
RGD	XRGDX	Fibronectin, osteopontin, BSP and others
pRGD / bsp-RGD	CGNGEPRGDTYRAY	BSP
hBSP ₂₇₈₋₂₉₃	YESENGEPRGDNYRAY	BSP
PHSRN	PHSRN	Fibronectin
F105	YKRSRYT	FGF-2
F119	KRTGQYKLGSKTGPQK	FGF-2
F36	PDGRVD	FGF-2
F77	KEDGRLL	FGF-2
GFOGER	GGYGGGPC(GPP) ₂ GFOGER(GPP) ₂ GPC	Collagen type I
DGEA	DGEA	Collagen type I
P15	GTPGPQGIAGQRGVV	Collagen type I
AC-100	ERGDNDISPFSGDQ	MEPE
ODP (osteopontin-derived peptide)	DVDVDPDRGDSLAYG	Osteopontin
RRETAWA	RRETAWA	Identified by phage display
YIGSR	YIGSR	Laminin
IKVAV	IKVAV	Laminin
Ln2-P3	DLTIDDSYWYRI	Laminin
KRSR	KRSR	BSP, fibronectin, osteopontin and others
Consensus heparin binding domain	FHRRIKA	BSP
HBD peptide	RKKNPNCRRH	BMP-4
BMP-2-derived peptide	NSVNSKIPKACCVPELSAI	BMP-2
BMP-2-derived peptide	KIPKASSVPELSAISTLYL	BMP-2
P24	S ^[PO4] KIPKASSVPELSAISTLYLDDDD	BMP-2
pBMP-9 / SpBMP-9	CGGKVGKA(CC/SS)VPTKLSPIVLYK	BMP-9
BMP-9-derived peptide	RKVGKASSVPTKLSPIVLYK	BMP-9
BMP-7-derived peptide	RTVPKPSSAPTQLNAISTLYF	BMP-7
BFP-1	GQGFSPYKAVFSTQ	BMP-7
OPD (osteopromotive domain)	DWIVA	BMP-2
CBM	GLRSKSKFRRPDIQYPDATDEDITSHM	Osteopontin
BCSP TM -1	NGLPGPIGP	Collagen type I
OGP (osteogenic growth peptide)	ALKRQGRRTLYGFGG	Naturally occurring
OGP ₁₀₋₁₄	YGFGG	OGP
PTH ₁₋₃₄	SVSEIQLMHNLGKHLNSMERVEWLRKQLQDVHNF	Parathyroid hormone
CB	NGVFKYRPRYLYKHAYFYPHLKRFPVQ	BSP
CTC peptide	IAGVGGKESGGF	Collagen IIIa
Substance P	RPKPQQFFGLM	Naturally occurring
Endothelin-1	CSCSSLMDKECVYFCHLDIHW	Naturally occurring
QK	KLWQELYQLKYKGI	VEGF
PBA2-1c	(CVRKIEIVRKK) ₂ -Ahx-Ahx-Ahx-RKRKLERIAR	PDGF
Exendin 4	HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS	Glucagon-like peptide
OPD (osteopontin-derived peptide)	SVVYGLR	Osteopontin
SPARC 113	TLEGTKKGHLHLDY	Osteonectin
SPARC 118	KKGHK	Osteonectin
TP508	AGYKPDGKRGDACEGDSGGPFV	Thrombin
RoY	YPHIDSLGHWRR	Designed
LL-37	LLGDFFRKSKEKIGKEFKRIVQRIKDFLRNLPRTES	hCAP18



peptides derived from ECM proteins
adhesion vs. other bioactivities

RGD - PHSRN	YIGSR	P-15
DGEA		GFOGER

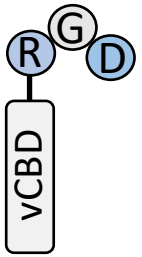
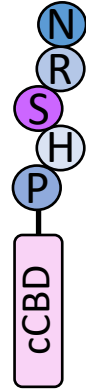
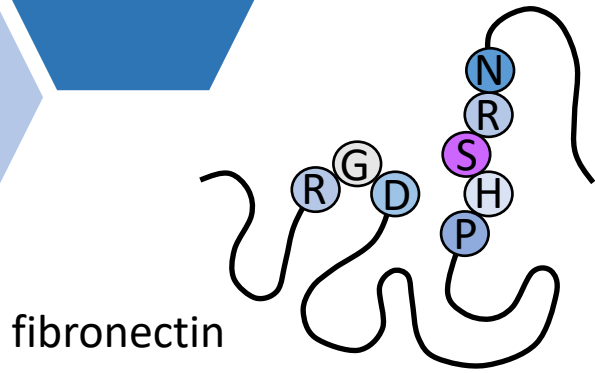
other peptides
natural peptides, hormone-derived
peptides, cathelicidins
PTH₁₋₃₄ (teriparatide)



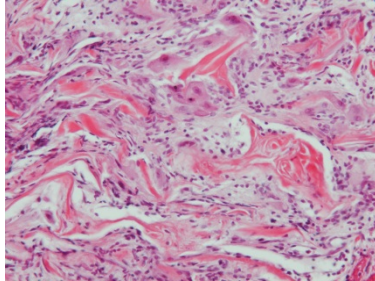
peptides derived from BMPs
chondro- / osteoinduction

Peptides derived from angiogenic factors
angiogenesis

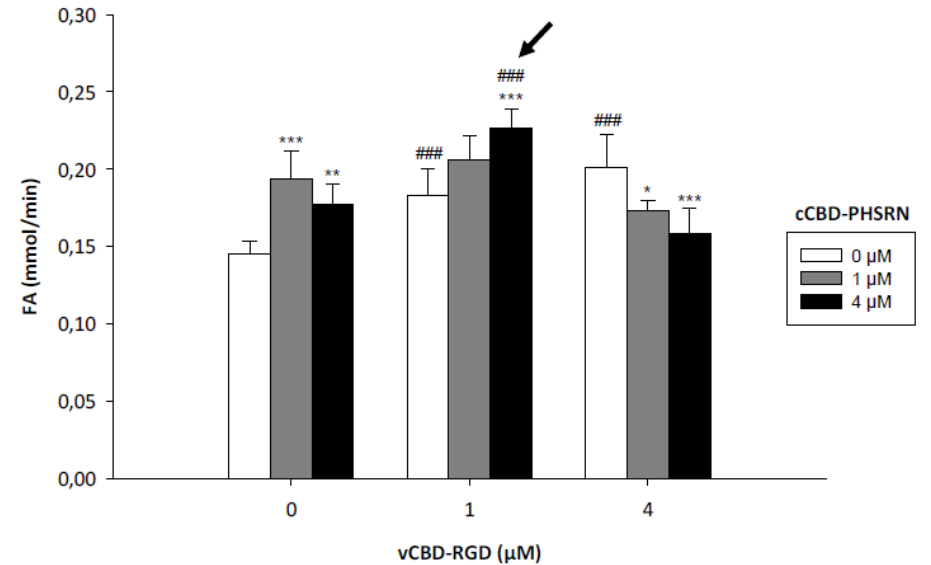
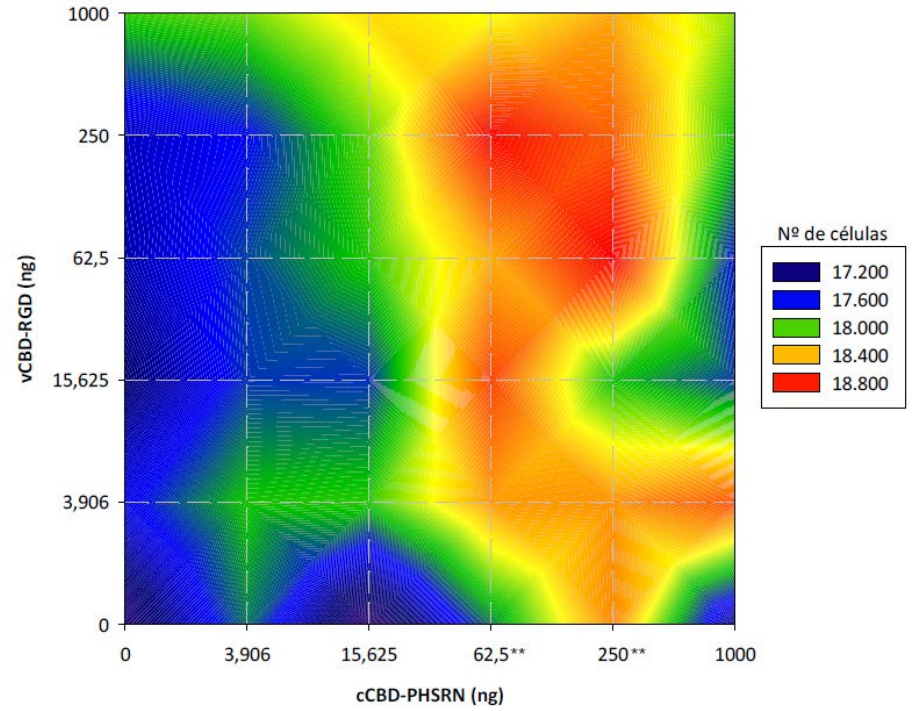
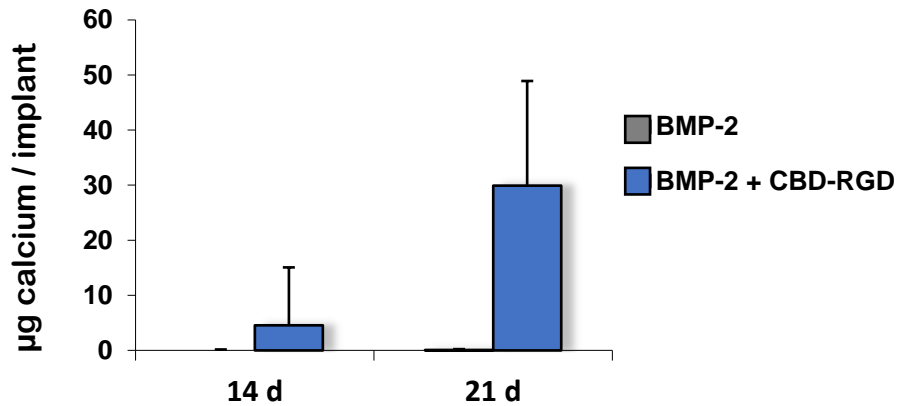
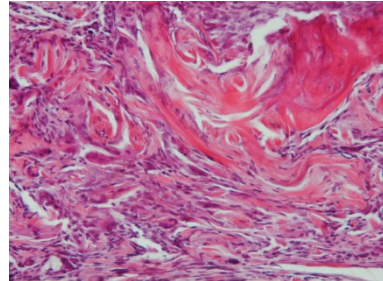
A personal experience



BMP-2



BMP-2 + CBD-RGD



Visser *et al.*, 2014
 Visser *et al.*, 2016
 Rico-Llanos, 2018