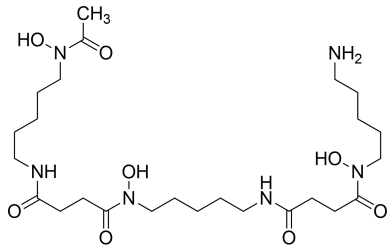
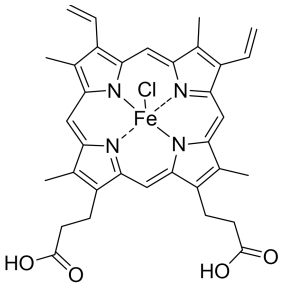
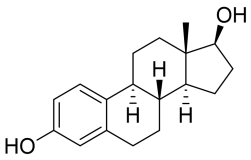
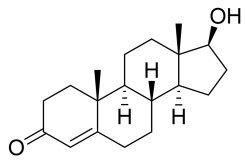
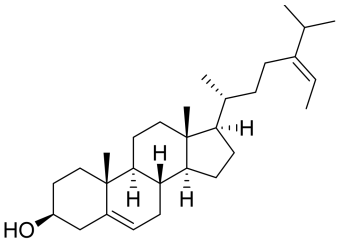
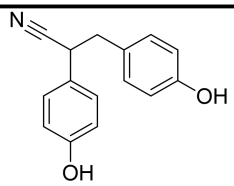
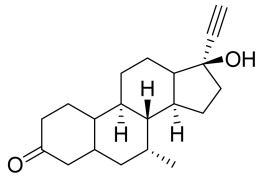
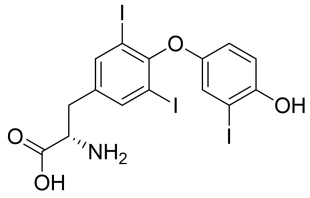
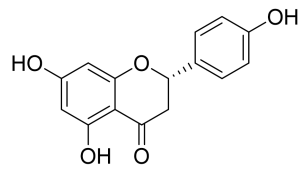
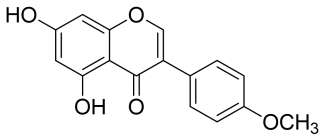
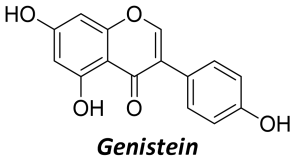
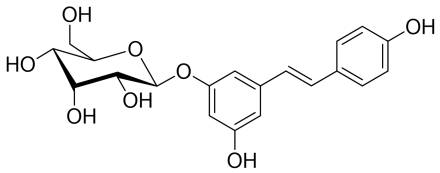
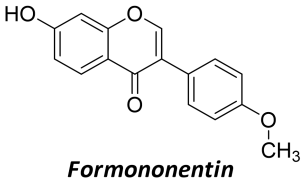
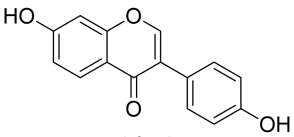
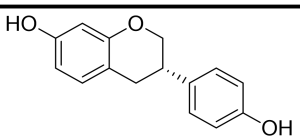
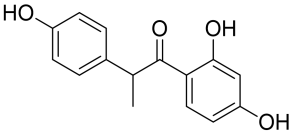
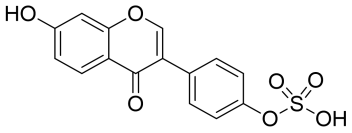
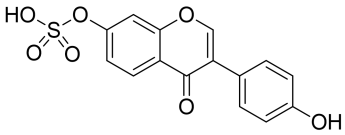
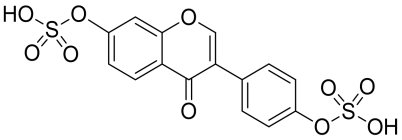
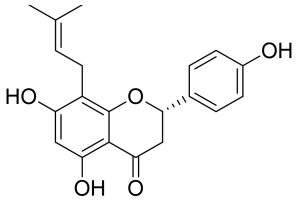
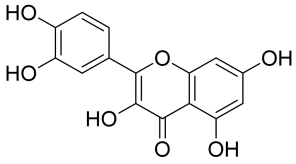
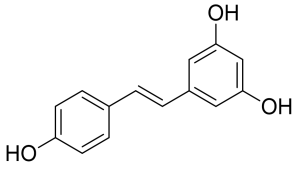
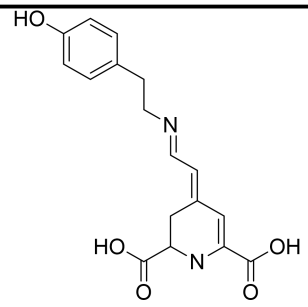
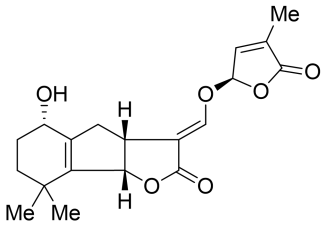
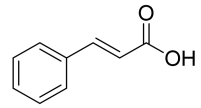
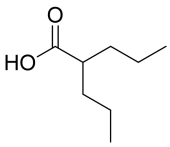
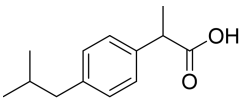
Additional Table 1 Natural and synthetic compounds as Ngb pharmacological modulators

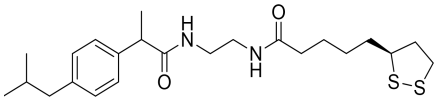
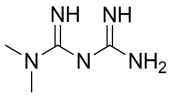
Molecule	Model			Clinical use	Reference
	Primary cultured neurons	*In vivo*	Non-neuronal cultured cells		
Iron chelators					
Synthetic					
 ***Deferoxamine***	SK-N-BE cells mRNA ↑ Ngb ↑			Iron overload	Sun et al. (2001)
Natural					
 ***Hemin***	HN33 cells mRNA ↑ Ngb ↑	C57BL/6 mice (Retina) mRNA ↑ Ngb ↑		Porphyria	Zhu et al. (2002); Tao et al. (2018)
Hormones and derivatives					
Steroids and analogues					
Naturals					
 ***17-beta-estradiol***	SK-N-BE cells, astrocytes mRNA ↑ Ngb ↑		MCF-7, HepG2 mRNA ↑ Ngb ↑	Menopause hormone therapy	De Marinis et al. (2010); Fiocchetti et al. (2014); De Marinis et al. (2013a)

 ***Testosterone***	T98G cells mRNA n.d. Ngb ↑		Hormonal deficiency	Toro-Urrego et al. (2016)
 ***Fucosterol***		SH-SY5Y cells mRNA ↑ Ngb n.d.	n.d.	Gan et al. (2019)
Synthetic				
 ***Diarylpropionitrile***	SN-K-BE mRNA ↑ Ngb ↑		n.d.	De Marinis et al. (2010)
 ***Tibolone***	T98G cells mRNA ↑ Ngb ↑		Menopause hormone therapy	Avila-Rodriguez et al. (2016)
Thyroid hormone				
 ***Triidothyronine***		Male rats' hippocampus, cerebellum and cortex mRNA ↑ Ngb ↑	Early stages of hypothyroidism	Oliveira et al. (2015)
Plants derivatives				
Polyphenolics compounds				

 ***Naringenin***	SK-N-BE mRNA n.d. Ngb ↑	MCF-7 mRNA n.d. Ngb no change	n.d.	De Marinis et al. (2010); Cipolletti et al. (2019)
 ***Biochanin A***	N2a, SKNSH mRNA ↑ Ngb ↑		n.d.	Liu et al. (2016)
 ***Genistein***	N2a, SKNSH mRNA ↑ Ngb ↑	MCF-7 mRNA n.d. Ngb no change	n.d.	Liu et al. (2016); Cipolletti et al. (2019)
 ***Polydatin***	N2a, SKNSH mRNA ↑ Ngb ↑		n.d.	Liu et al. (2016)
 ***Formononentin***	N2a, SKNSH mRNA ↑ Ngb ↑		n.d.	Liu et al. (2016)
 ***Daidzein***	N2a, SKNSH mRNA ↑ Ngb ↑	MCF-7, T47D mRNA n.d. Ngb ↓	n.d.	Liu et al. (2016); Montalesi et al. (2020)
 ***Equol***		MCF-7, T47D mRNA n.d. Ngb ↑	n.d.	Montalesi et al. (2020)
 ***o-desmethylangolensin***		MCF-7, cells mRNA n.d. 0,1 µmol Ngb ↑,	n.d.	Montalesi et al. (2020)

		1 μmol no change		
 *Daidzein 4-Sulfate*		MCF-7, T47D mRNA n.d. Ngb ↓	n.d.	(Montalesi et al., 2020)
 *Daidzein 7-Sulfate*		MCF-7 mRNA n.d. Ngb ↑	n.d.	Montalesi et al. (2020)
 *Daidzein 4,7-disulfate*		MCF-7 mRNA n.d. 0,1-1μmol Ngb ↑ 1 μmol no change	n.d.	Montalesi et al. (2020)
 *8-Prenylnaringenin*		MCF-7 mRNA n.d. Ngb ↑	n.d.	Cipolletti et al. (2019)
 *Quercetin*		MCF-7 mRNA n.d. Ngb ↑	n.d.	Cipolletti et al. (2019)
 *Resveratrol*	SK-N-BE mRNA n.d. Ngb ↑	MCF-7 mRNA n.d. Ngb no change	n.d.	Cipolletti et al. (2019)

Other plants derivatives				
 *Miraxanthin-III*		Molecular docking mRNA n.d. Ngb n.d.	n.d.	Pangestu et al. (2018)
 *Strigol*		Molecular docking mRNA n.d. Ngb n.d.	n.d.	Pangestu et al. (2018)
Short-chain fatty acids				
Natural				
 *Trans-Cinnamic Acid*	HN33 cells	mRNA ↑ Ngb ↑	n.d.	Jin et al. (2011)
Synthetic				
 *Valproic Acid*	HN33 cells	mRNA ↑ Ngb ↑	Anticonvulsant drug	Jin et al. (2011)
NSAIDs				
Synthetic				
 *Ibuprofen*	AD rats	mRNA n.d. Ngb ↑	NSAIDs	Zara et al. (2013)

 *Ibuprofen-lipoic acid*	AD rats mRNA n.d. Ngb ↑	NSAIDs	Zara et al. (2013)
Antidiabetic			
Synthetic			
 *Metformin*	Wistar rats with alcohol-induced neurotoxicity mRNA n.d. Ngb ↑	Antidiabetic drug	Bonea et al. (2020)

AD: Alzheimer's disease; n.d.: not detected; Ngb: neuroglobin; NSAIDs: nonsteroidal anti-inflammatory drugs