THERAPEUTIC POTENTIAL OF TARGETING PROKINETICIN RECEPTORS IN DISEASES

Martina Vincenzi, Amin Kremić, Appoline Jouve, Roberta Lattanzi, Rossella Miele, Mohamed Benharouga, Nadia Alfaidy- Benharouga, Stephanie Migrenne-Li, Anumantha G. Kanthasamy, Marimelia Porcionatto, Napoleone Ferrara, Igor V. Tetko, Laurent Désaubry, Canan G. Nebigil*

Regenerative Nanomedicine (UMR 1260), INSERM, University of Strasbourg, Center of Research in Biomedicine of Strasbourg, 1 Rue Eugène Boeckel, 67000, Strasbourg, France (M.V., A.K., A.J., L.D., C.G.N.); Department of physiology and pharmacology "Vittorio Erspamer", Sapienza University of Rome, 00185 Rome, Italy (M.V., R.L.); Department of biochemical sciences "Alessandro Rossi Fanelli", Sapienza University of Rome, 00185 Rome, Italy (R.M.); University Grenoble Alpes, INSERM, CEA, U1292 BIOSANTE, 38000 Grenoble (M.B. and N.A.); Unité de Biologie Fonctionnelle et Adaptative, Université Paris Cité, CNRS, 75013 Paris, France (S.M.); Department of Physiology and Pharamacology, Center for Neurological Disease Research, University of Georgia, Athens, GA, USA (A.G.K.); Department of Biochemistry, Escola Paulista de Medicina, Universidade Federal de São Paulo (M.A.P.); Moores Cancer Center, University of California, San Diego, La Jolla, CA (N.F.); Institute of Structural Biology, Helmholtz Munich - German Research Center for Environmental Health (GmbH), Ingolstädter Landstraße 1, 85764 Neuherberg, Germany (I.V.T.).

Table S1. Mutations in the Prokineticin 1 and 2 (PK1 and PK2) and their receptors PKR1 and PKR2 may lead to several diseases

Pathology	PK1 DNA mutation (c.)	PK1 protein mutation (p.)	Reference
Hirschsprung's disease	-45G>A 142C>T 162G>T	R48W 654G*	(Ruiz-Ferrer et al., 2011)
Recurrent miscarriage		V76I	(Su et al., 2016)
Leber's hereditary optic neuropathy	199G>A		(Cheng et al., 2022)
Pathology	**PK2 DNA mutation (c.)**	**PK2 protein mutation (p.)**	**Reference**
	4C>A		(Dodé et al., 2006)
	70G>C	A24P	(Cole et al., 2008)
	94G>C	G32R	(Dodé et al., 2006)
	101G>A	C34Y	(Cole et al., 2008)
	122G>T	G41D	(Quaynor et al., 2011)
	137G>A	C46Y	(Dodé and Rondard, 2013)
	150C>G	I50M	(Cole et al., 2008)

Kallmann syndrome	161G>A	S54N	(Dodé and Hardelin, 2009)
	163delA	I55fsX1	(Leroy et al., 2008; Pitteloud et al., 2007)
	217C>T	R73C	(Cole et al., 2008; Dodé et al., 2006; Leroy et al., 2008)
	223-4C>A		(Zhou and Li, 2021)
	234_235insT	79fsX100	(Dodé et al., 2006)
	297_298insT	G100fsX121	(Abreu et al., 2008)
	297_299insT	G100fsX22	(Abreu et al., 2008; Dodé et al., 2006)
	301C>T 302C>T	R101W R101Q	(Dodé and Rondard, 2013)
	309G>A	M103I	(Alkelai et al., 2017)
	310C>T	H104Y	(Dodé and Hardelin, 2009)
	364C>T	R122X	(Sarfati et al., 2013)
		C383FfsX1	(Libri et al., 2014)
Normosmic congenital hypogonadotropic hypogonadism	349C>T	R117W	(Pablo Méndez et al., 2015)
Congenital hypogonadotrophic hypogonadism	68G>A	R23H	(Ayers et al., 2017)
		C46F	(Moya-Plana et al., 2013)
Normosmic idiopathic hypogonadotropic hypogonadism	1A>C	M1L	(Çiftci et al., 2023)
	163delA	I55fsX1	(Pitteloud et al., 2007)
	217C>T	R73C	(Cole et al., 2008)
	223-4C>A 306G>C	R102S	(Liu et al., 2022)
Pathology	**PKR1 DNA mutation (c.)**	**PKR1 protein mutation (p.)**	**Reference**
Hirschsprung's disease	387C>T 1062A>T 1121G>A	S129S K354N L374L	(Ruiz-Ferrer et al., 2011)
Recurrent miscarriage		I379V	(Su et al., 2014)
Pathology	**PKR2 DNA mutation (c.)**	**PKR2 protein mutation (p.)**	**Reference**
Kallmann syndrome	57delC		(Quaynor et al., 2011)
	58delC	20fsX43 20fsX24	(Dodé et al., 2006) (Sarfati et al. 2010)
	125_126insTGAGGA	42insED	(Zhao et al., 2019)
	151G>A	A51T	(Dodé and Rondard, 2013)
	163G>A	V55I	(Quaynor et al., 2011; Sugisawa et al., 2022)
	238C>T	R80C	(Abreu et al., 2008)
	253C>T	R85C	(Cole et al., 2008; Monnier et al., 2009)
	253C>G	R85G	(Sarfati et al., 2010)
	254G>T	R85L	(Dodé and Hardelin, 2009)
	254G>A	R85H	(Dodé et al., 2006; Monnier et al., 2009)
	308C>T	A103V	(Ma et al., 2022)
	337T>C 343G>A	Y113H V115M	(Cole et al., 2008)
	349C>T	R117W	(Dodé and Rondard, 2013)
	403C>T	R135C	(Gach et al., 2020)
	420C>G	Y140X	(Abreu et al., 2008)
	472G>A	V158I	(Libri et al., 2014)

	491G>A	R164Q	(Cole et al., 2008; Dodé et al., 2006; Monnier et al., 2009)
	518T>G	L173R	(Abreu et al., 2008; Cole et al., 2008; Dodé et al., 2006; Monnier et al., 2009)
	533G>C	W178S	(Cole et al., 2008; Dodé et al., 2006; Monnier et al., 2009)
	561_563dup	S188dup	(Danda et al., 2020)
	563C>T	S188L	(Cole et al., 2008)
	629A>G	Q210R	(Dodé et al., 2006; Monnier et al., 2009)
	691G>A	E231K	(Zhao et al., 2019)
	701G>A	G234D	(Dodé and Rondard, 2013)
	728A>G	T243C	(Gach et al., 2020)
	743G>A	R248Q	(Cole et al., 2008)
	752G>T	W251L	(Sarfati et al., 2010)
	779C>T	T260M	(Libri et al., 2014)
	802C>T	R268C	(Abreu et al., 2008; Dodé et al., 2006; Monnier et al., 2009)
	820T>A	V274D	(Libri et al., 2014; Sinisi et al., 2008)
	868C>T	P290S	(Dodé et al., 2006; Monnier et al., 2009)
	969G>A	M323I	(Dodé et al., 2006; Monnier et al., 2009)
	989delC	T330fsX5	(Sarfati et al., 2010)
	991G>A	V331M	(Cole et al., 2008; Dodé et al., 2006; Monnier et al., 2009)
	1058G>A	R353H	(Zhao et al., 2019)
	1069C>T	R357W	(Cole et al., 2008)
		V331Cfs*4 H20MfsTer24	(Sugisawa et al., 2022)
Normosmic idiopathic hypogonadotropic hypogonadism	43insACTTT 56delC	N15fsX30 H20MfsX23	(Libri et al., 2014) (Libri et al. 2014)
	253C>T	R85C	(Cole et al., 2008)
	337T>C	Y113H	(Zhao et al., 2019)
	472G>A	V158I	(Wang et al., 2022)
	491G>A 518T>G	R164Q L173R	(Quaynor et al., 2011)
	533G>C	W178S	(Cole et al., 2008; Zhao et al., 2019)
	563C>T	S188L	(Cole et al., 2008)
	614_616del	K205del	(Mkaouar et al., 2021)
	653T>C 685G>C	L218P G229R	(Zhao et al., 2019)
	743G>A	R248Q	(Cole et al., 2008)
	802C>T	R268C	(Libri et al., 2014)
	809G>A	R270H	(Zhao et al., 2019)
	891_892insA	R298Tfs*2	(Zhou et al., 2022)
	1000G>A	V334M	(Libri et al., 2014)
Congenital hypogonadotropic hypogonadism		G57C	(Li et al., 2021)
	337T>C	Y113H	(Zhang et al., 2021)
	533G>C	W178S	(Li et al., 2021; Zhang et al., 2021)
	563C>T	S188L	(Ayers et al., 2017)

	685G>C 725C>T 790C>T 852A>T 864G>A 889G>A	G229R P242L R264C Y284C W288X V297I	(Li et al., 2021)
	991G>A 1054T>G	V331M W352G	(Ayers et al., 2017)
	1111G>A	G371A	(Li et al., 2021)
	308C>T	A103V D42delinsDED	(Xie et al., 2022)
		W212* Y113H M111R T340S	(Sugisawa et al., 2022)
Congenital hypopituitarism	691G>A	E231K	(Vishnopolska et al., 2021)
	151>GA 254G>T 518T>G 802C>T	A51T R85L L173R R268C G371R	(McCabe et al., 2013)
Central precocious puberty	8-40C>T 458+62G>A 465C>T 525C>G 585G>C		(Aiello et al., 2021)
	724_727delTGCT	C242fsX305	(Fukami et al., 2017)
Combined pituitary hormone deficiency (CPHD)	56delC	H20MfsX23	(Libri et al., 2014)
	151G>A	A51T	(Asakura et al., 2015)
	253C>T	R85C	(Correa et al., 2015)
	253C>G 254G>A	R85G R85H	(Asakura et al., 2015)
	254G>T	R85L	(Bajuk Studen et al., 2019)
	742C>T	R248W	(Asakura et al., 2015)
	743G>A	R248E	(Correa et al., 2015)
	779C>T 991G>A	T260M V331M	(Libri et al., 2014)
Isolated GnRH deficiency (IGD)		M64V D112Y S202G R270C V317L N325K	(Cox et al., 2018)
Hirschsprung's disease	202G>A 253C>T 254G>A 802C>T 868C>T 876C>T 889G>A	G68S R85C R85H R268C P290S Y292Y V297I	(Ruiz-Ferrer et al., 2011)

Pituitary stalk interruption syndrome	151G>A	A51T	(Wang et al., 2017)
	991G>A 1057C>T	V331M	(Han et al., 2016)
Recurrent miscarriage		V331M	(Su et al., 2013)

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