



SUPPLEMENTARY MATERIALS

A Bioinformatics Model of Human Diseases on the basis of Differentially Expressed Genes (of Domestic versus Wild Animals) That Are Orthologs of Human Genes Associated with Reproductive-Potential Changes

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Supplementary data on effects of the human gene underexpression or overexpression under this study on the reproductive potential

Table S1. Effects of underexpression or overexpression of the human genes under this study on the reproductive potential according to our estimates [1-5].

щ.	Human	Deficit (↓)				Excess (↑)				
#	Gene	Nsnp	Effect on reproductive potential [Reference]	ďŶ	Nsni	P Effect on reproductive potential [Reference]	ď₽			
1	ACKR1	1 [3]	increased risks of preeclampsia as one of the most challenging problems of modern obstetrics [8]	←		increased risk of atherosclerosis and other coronary artery disease [9]	←			
2	ADCYAP1	1 [4]	within a model of human diseases using Adcyap1-knockout mice, decreased fertility [10]	\leftarrow	3 [4]	in a model of human health using transgenic mice overexpressing Adcyap1 within only pancreatic β-cells, ameliorated diabetes [11]	\rightarrow			
3	ADCYAP1R1	2 [4]	within a model of human diseases using Adcyap1r1-knockout female mice, decreased fertility [12]	<i>—</i>	4 [4]	increased risks of increased chronic post-traumatic nociceptive pain- related behavior [13]	\leftarrow			
4	ADORA1	5 [4]	within a model of human fertility using Adora1-knockout male mice, delayed sperm maturation and, ultimately, fewer offspring [14]	←	5 [4]	in a human health model using norm rather than Adora1-knockout mice, Adora1-agonist improves post-ejaculation sperm ripening [15]	\rightarrow			
5	ADORA2A	3 [4]	within a model of human diseases using adult male mice, predisposition to fearfulness, helplessness, and fatigue [16]	←	10 [4]	within a model of human diseases using mice, improved survival in post-traumatic endotoxemia and sepsis [17]	\rightarrow			
6	ADORA2B		in models of men fertility using mice, increased risks of insufficiencies in maturation and storage of spermatozoa within epididymis [18]	←	1 [4]	within a model of human diseases using mice, increased risks of voluntary physically-inactive behavior [19]	←			
7	ADORA3	2 [4]	within a model of human diseases using Adora3-knockout mice, platelet deficit with bleeding without blood coagulation in trauma [20]	←	9 [4]	within models of human diseases using mice, chronic pain insensitivity [21]	$^{\prime} \rightarrow$			
8	ADRA1A	2 [4]	within a model of human diseases using ADRA1A-knockout mice, twice reduced pregnancy rate [22]	←	9 [4]	within a model of human diseases using mice carrying constitutively more bioactive ADRA1A-mutant, antidepressant-like behavior [23]	\rightarrow			
9	ADRA1D		within a model of human diseases using triple ADRA1A-, ADRA1B-, and ADRA1D-knockout mice, drastic reduced pregnancy rate [22]	\leftarrow	1 [4]	reduced risks of muscle atrophy after trauma and diseases, as well as during ageing [24]	\rightarrow			

<u>Note</u>: NSNP, as the number of candidate SNP markers that significantly decrease or increase the affinity of the TATA-binding protein (TBP) for the promoters of the considered gene according to estimates cited as [Ref] and, thereby, decrease (\downarrow) or increase (\uparrow) the expression of this gene, as has been repeatedly proven by many independent experiments (e.g., [6], for a review, see [7]); σ ?, as effects on human reproductive potential: deterioration (\leftarrow) or improvement (\rightarrow). <u>Genes</u>: *ACKR1*, atypical chemokine receptor 1 (synonym: Duffy blood group); *ADCYAP1*, adenylate cyclase activating polypeptide 1; *ADCYAP1R1*, pituitary adenylate cyclase-activating polypeptide type 1 receptor; *ADORA1*, *ADORA2A*, *ADORA2B*, and *ADORA3*, adenosine receptors A1, A2a, A2b, and A3, respectively; *ADRA1A and ADRA1D*, adrenoceptors α 1A. and α 1D, respectively,

щ	Human		Deficit (↓)		Excess (↑)		
Ħ	Gene	Nsnp	Effect on reproductive potential [Reference]	ď₽	Nsn	P Effect on reproductive potential [Reference]	ď₽
10	ADRA2C		in human disease models using Adra2c-knockout mice, higher startle responses, lesser startle reflex inhibition and attack-respond delay [25]	~	2 [4]	in human disease models using Adra2c-excessive mice, lesser startle responses, more startle reflex inhibition and attack-respond delay [25]	
11	ADRB2	2 [4]	within models of human fertility using aging female rats, propranolol blocks Adrb2 and thus successfully prolongs their reproductive age [26]	\rightarrow		within models of human fertility using aging female rats, the age- induced increase of Adrb2 level reduces their fertility indicators [26]	←
12	ADRB3		in a model of human behavior using Adrb3-knockout mice, resistance to antidepressant-treatment against post-stress worsen physical state [27]	~	1 [4]	within models of human diseases using rats and mice, synthetic Adrb3-agonist SR58611A causes antidepressant-like behavior [28]	\rightarrow
13 2	AKAP17A	6 [5]	predisposition to accelerated aging in men [29]	\leftarrow	13 [5]	increased risk of azoospermia through testicular degeneration [30]	←
14	AMELY	1 [5]	increased risk of suicide in men [31]	←		exogenous recombinant amelogenin is a wound healing drug [32]	\rightarrow
15	APOA1	1 [3]	increased risk of mental disorders according to low score of Montreal Cognitive Assessment (MoCA) [33]	←		unexplained infertility in women [34]	←
16	AR		increased risk of early mortality through metabolic diseases because of disturbed gut microbiota [35]	←	3 [3]	androgen-induced premature aging in adult men [36]	←
17	ARTN	3 [4]	within a model of human embryogenesis using mouse embryos, impaired neurotrophic support of tissue innervation [37]	l ←	9 [4]	in models of human behavior using Artn-knockdown mice, exogenous Artn has antidepressant-like effect at 30 min after administration [38]	
18	ASMT	3 [5]	increased risks of inflammatory airway diseases such as asthma because of melatonin deficiency [39]	f ←	10 [5]	melatonin excess protects sperm from oxidative DNA damage [40]	\rightarrow
19	ASMTL	5 [5]	increased risk of prostate cancer [41]	←	13 [5]	increased risk of autism spectrum disorders [42]	←
20	AVPR1A		within a model of human pregnancy using Avpr1a-deficient female mice, fewer pups, labor initiation delay, stronger postpartum bleeding [43]	←	2 [4]	within a human cohort-based comparative clinical study, increased risks of depression-like behavior [44]	←
21	AVPR2	1 [4]	within a model of human preeclampsia using co-infusion of vasopressin with Avpr2-antagonist into mice, prevented fetal growth restriction [45]	\rightarrow	1 [4]	in human preeclampsia models using gravid mice norm injected by only vasopressin without Avpr2-antagonist, reduced fetal mass [45]	←
22	BDNF	4 [4]	within a female human cohort-based comparative clinical study, increased risks of both moderate and severe depressive behavior [46]	¹ ←	10 [4]	within retrospective meta-analysis of BDNF-related publications in- between January 2018 and February 2019, better woman fertility [47]	\rightarrow
23	CC2D1A		in human disease models using mice with either knockout or conditional knockdown of Cc2d1a, perinatal lethality or cognitive deficit, respectively [48]] ←	6 [2]	increased risks of both anxious and depressive behavior [49]	←
24	CC2D1B	4 [2]	within a model of human diseases using Cc2d1b-knockout mice, increased risks of cognitive deficit [50]	←	8 [2]	within human behavior models using rats, increased level of fear- induced aggressive response [51]	\rightarrow
25	CD99	3 [5]	anti-CD99 drugs retard atherogenesis that reduce risks of stroke and myocardial infarction as two most often causes of human death [52]	\rightarrow	20 [5]	increased mortality from septic shock in men [53]	←
26	CDNF	1 [4]	within a model of human diseases using CDNF-knockout mice, increased risks of degenerated enteric neurons [54]	←	4 [4]	within human disease models using exogenous CDNF injected into normal mice brain, prevented dopaminergic neuron degeneration [55]	$] \rightarrow$

<u>Genes</u>: ADRA2C, ADRB2, and ADRB3, adrenoceptors α2C, β2, and β3, respectively; *AKAP17A*, A-kinase anchoring protein 17A; *AMELY*, amelogenin Y-linked; *APOA1*, apolipoprotein A1; *AR*, androgen receptor; *ARTN*, artemin; *ASMT*, acetylserotonin O-methyltransferase; *ASMTL*, N-acetylserotonin O-methyltransferase-like protein; *AVPR1A* and *AVPR2*, arginine vasopressin receptors 1A and 2, respectively; *BDNF*, brain derived neurotrophic factor; *CC2D1A* and *CC2D1B*, Freud-1 and Freud-2, respectively; *CD99*, CD99 molecule (synonym: Xg blood group); *CDNF*, cerebral dopamine neurotrophic factor.

" Human		Deficit (↓)			Excess (↑)	
[#] Gene	Nsnp	Effect on reproductive potential [Reference]	σŶ	Nsnp	Effect on reproductive potential [Reference]	ď₽
27 CDY2A	1 [5]	male maturation arrest [56]	\leftarrow		partly repaired fertility in men, who have AZFc-deletion containing the CDY1 gene-paralog necessary to finalize spermatogenesis [57]	\rightarrow
28 CETP	1 [3]	retarded atherogenesis that reduce risks of both stroke and myocardial infarction as two most often causes of human death [58]	\rightarrow	3 [3]	increased risks of hypercholesterolemia in late pregnancy [59]	←
29 CHRM1	1 [4]	within a model of human diseases using Chrm1-knockout mice, larger pancreatic intraepithelial neoplasia area and shorter overall survival [60]	←	1 [4]	increased risks for chronic fatigue syndrome [61]	\leftarrow
30 CHRM2	1 [4]	within a model of human diseases using rats inoculated by Japanese encephalitis virus, worse spatio temporal learning and memory [62]	←	2 [4]	within a human cohort-based clinical study, improved susceptibility to antidepressant mood stabilizers in depressive disorders [63]	←
31 CHRM3		within a model of human post-injury cure using human neurons, CHRM3- antagonist improved oligodendrocyte repair in brain and spinal cord [64]	\rightarrow	1 [4]	within a human cancer cell clinical study ex vivo, increased risks of benign prostatic hyperplasia as a prostate disease precursor [65]	←
32 CHRM4	1 [4]	within a model of human diseases using rats, increased risks of both acute and chronic arthritis [66]	←	2 [4]	within clinical study using cell lines of prostate cancer vs norm, increased risks of neuroendocrine prostate cancer [67]	←
33 CHRM5	1 [4]	based on a clinical case of patient carrying <i>de novo</i> interstitial 5,3 Mb-deletion of chromosome 15 containing <i>CHRM5</i> , raised risks of mental retardation [68]		4 [4]	in human behavior models using mice, antidepressant imipramine upregulated CHRM5 to treat for chronic stress complications [69]	\rightarrow
34 CHRNA1	1 [4]	within a model of human neuromuscular hyperactivity complications using zebrafish, motor axonal extension and muscular degeneration [70]	←	2 [4]	in human amyotrophic lateral sclerosis models using mice: skeletal gastrocnemius, quadriceps and soleus muscles denervation [71]	←
35 CHRNA2		in human pregnancy models using Chrna2-null mice, prevented negative effects of maternal nicotine exposure on learning and memory in pups [72]	\rightarrow	7 [4]	within clinical study of pedigree segregating sleep-related epilepsy: higher risk of seizures, fear sensation, and nocturnal wanderings [73]	→
34 CHRNA3	2 [4]	within a model of human diseases using songbirds, improved finding an opposite sex tribesman [74]	\rightarrow		enhanced adverse effects of nicotine compounds on primordial oocytes [75]	←
35 CHRNA4		within a model of human behavior using Chrna4-knockout mice, increased risks of anxiety [76]	←	13 [4]	within a model of human diseases using mice, increased risks of congestive heart failure [77]	←
36 CHRNA5	4 [4]	within a model of human cord brain injury using Chrna5-knockdown rats, relieved mechanical pain [78]	\rightarrow	5 [4]	within a model of human cord brain injury using rats, hypersensitivity to mechanical pain [78]	←
37 CHRNA6	2 [4]	enhanced maternal behavior [79]	\rightarrow		within a model of human diseases using mice, increased risks of both neuropsychiatric disorders and social defeats [80]	←
38 CHRNA7	2 [4]	within a model of human behavior using mice administered by Chrna7- antagonist, improved antidepressant-like behavior [81]	\rightarrow	2 [4]	according to the retrospective exhaustive review, behavioral and cognitive benefits compared to norm due to excessive Ca(2+) ions [82]	\rightarrow
39 CHRNA9	1 [4]	in human pain models using Chrna9-knockout mice, both the development and maintenance of chronic mechanical hyperalgesia were reduced [83]	\rightarrow	1 [4]	based on the bioinformatics meta-analysis of microarray datasets from ArrayExpress database, increased risks of gliomas and glioblastoma [84]	→
40 CHRNA10	1 [4]	in human pain sensitivity models using adult male rats administered by Chrna10-antagonist, chronic neuropathic hyperalgesia reduced [85]	\rightarrow	1 [4]	in human viability models using human and rat blood cells stimulated with Chrna10-agonists, innate immune response estimate reduced [86]	\rightarrow
41 CHRNB1	3 [4]	based on the family history of calves carrying "Chrna1-loss of function" gene: increased risks of neuromuscular disorders and fetal lethality [87]	~	3 [4]	within a model of human motor activity using mice, reduced muscle size with increased efficiency of muscle functioning [88]	\rightarrow

<u>*Genes:*</u> CDY2A, chromodomain Y-linked 2A; CETP, cholesteryl ester transfer protein; CHRM1, CHRM2, CHRM3, CHRM4, and CHRM5, cholinergic muscarinic receptors 1, 2, 3, 4, and 5, respectively; CHRNA1, CHRNA2, CHRNA3, CHRNA4, CHRNA5, CHRNA6, CHRNA6, CHRNA7, CHRNA9, CHRNA10, and CHRNB1, cholinergic nicotinic receptor subunits α1, α2, α3, α4, α5, α6, α7, α9, α10, and β1, respectively.

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#	Gene	Nsnp	Effect on reproductive potential [Reference]	ď₽	NSNPEffect on reproductive potential [Reference]\$
43 Cl	HRNB3	1 [4]	within a model of human depressive behavior using rats, increased risks of stress-induced both anhedonia and mood despair [89]	←	in human health models using Chrnb3-null mice, Chrnb3-excess may raises voluntary nicotine intake as a leading cause of preventable human death [90]
44 CI	HRNB4	3 [4]	within a model of human depressive behavior using rats, increased risks of stress-induced both anhedonia and mood despair [89]	←	 2 in human behavior models using transgenic mice carrying CHRNB4 on [4] bacterial artificial chromosome: reduced work memory & impulsiveness [91]
45 C	CHRNE		based on a case of a patient carrying genomic mutation reducing CHRNE level: predisposition to limb weakness and ophthalmoplegia [92]	←	 3 within a cohort-based clinical study of human myasthenia gravis: [4] predisposition to authoimmune-related muscle weakness [93]
46 C	HRNG	1 [4]	within a model of human embryogenesis using Chrng-knockout mice, increased risks of fetal lethality [94]	←	within a cohort-based clinical study, increased risks of rhabdomyosarcoma (embryonal rhabdomyosarcoma, 60% of cases) [95]
47 (CNR1	1 [4]	within a model of human behavior using Cnr1-knockout adult male mice, increased risks of anxiety and depression in men [96]	←	 6 in human behavior models using mice carrying artificial "gain-of- [4] function" mutation of Cnr1 gene: adolescent behavior in adulthood [97]
48 (CNTF	1 [4]	within a model of human behavior using Cntf-knockout mice, increased risks of both anxiety and depression [98]	←	in human post-injury vision repair models using CNTF-overexpressing neural stem cells injected into the mice eye injured, neuroprotection [99] \leftarrow
49 C	COMT	6 [4]	within a model of human behavior using the Comt-knockout female mice, increased risks of stress-induced both anxiety and depression [100]	←	 17 in human depression models using the Flinders Sensitive Line (FSL) of [4] rats, increased risks of anxiety and depressive-like behavior [101]
50 C	CRLF2	2 [5]	weakened symptoms of acute respiratory tract infections in children and the elderly [102]	\rightarrow	4 increased risks of B-cell acute lymphoblastic leukemia in children ← [5] [103]
51 C	SF2RA	9 [5]	Csf2ra-knockout mice (as models of human diseases using laboratory animals) have respiratory failure [104]	←	 4 lentiviral vectors carrying the mouse Csf2ra gene have passed [5] preclinical trials in mice for the treatment of respiratory failure [104] →
52 C	CXCR4	1 [4]	within a model of human behavior using CXCR4-null mice, increased risks of both motor coordination and balance impaired [105]	←	 3 in human behavior models using bee venom injection into rats, [4] development and maintenance of persistent pain hypersensitivity [106]
53 C	YP2A6	2 [3]	reduced damage from passive smoking for non-smoking pregnant women [107]	\rightarrow	Smilax china L. root extract increases CYP2A6 levels to detoxify → nicotine from tobacco smoke condensate in the lungs [108]
54 C	YP2B6	2 [3]	increased risk of hepatocellular carcinoma [109]	←	improved detoxification of toxins in the liver [110] \rightarrow
55 C Y	YP17A1	1 [3]	increased risk of reduced fertility [111]	←	 Malaysian propolis increases CYP17A1 level in the testes as a drug to overcome subfertility in diabetics [112] →
56 I	DHFR	3 [3]	DHFR-inhibitors are anti-mycobacterial drugs for tuberculosis [113]	\rightarrow	 2 increased risks of ectopic pregnancy, metastatic choriocarcinoma, and [3] gestational trophoblastic disease [114]
57 D	OHRSX	6 [5]	within a human disease model using HeLa cells, DHRSX knockdown reduces autophagy level as response to starvation [115]	←	3increased risk of stroke in men in middle age[5](i.e., reproductive age) [116]
58 D	NMT1	2 [3]	small doses of decitabine (a nucleoside analog) deplete the epigenetic DNMT1 regulator as a treatment for myeloid tumor [117]	\rightarrow	 7 within model of human disease using mice, increased risks of [3] epigenetic disorders of fetal brain development under stress [118]
59 1	DRD1		within a model of human embryogenesis using osteoblast-specific Ddr1- knockdown mice, reduced body weight and body length in newborns [119]	~	1 within a model of human behavior using adult male rats inoculated [4] with a lentiviral vector carrying DRD1 gene, more sexual activity [120] \rightarrow

<u>Genes</u>: CHRNB3, CHRNB4, CHRNE, and CHRNG, cholinergic nicotinic receptor subunits β3, β4, ε, and γ, respectively; CNR1, cannabinoid receptor 1; CNTF, ciliary neurotrophic factor; COMT, catechol-O-methyltransferase; CRLF2, cytokine receptor like factor 2; CSF2RA, colony stimulating factor 2 receptor subunit *α*; CXCR4, Fusin; CYP17A1, steroid 17α-monooxygenase; CYP2A6, xenobiotic monooxygenase; CYP2B6, 1,4-cineole 2-exo-monooxygenase; DHFR, dihydrofolate reductase; DHRSX, dehydrogenase/reductase X-linked; DNMT1, DNA methyltransferase 1; DRD1, dopamine receptors D1.

"Human		Deficit (↓)			Excess (↑)	
[#] Gene	Nsnp	Effect on reproductive potential [Reference] o	ç	Nsnp	Effect on reproductive potential [Reference]	ď₽
60 DRD2	3 [4]	within a model of human behavior using Drd2-knockout mice, decreased risks of depressive-like behavior [121]	→	10 [4]	within a model of human behavior using rats, increased risks of the chronic stress-induced depression-like behavior [122]	² ←
61 DRD3	1 [4]	in human behavior models using Drd3-null mice, increased risks of depression in those adult who were exposed to stress in childhood [123]	_	3 [4]	within a model of human behavior using mice, increased motor activity and behavior motivation [124]	\rightarrow
62 DRD4	1 [4]	within a model of human behavior using Drd4-knockout mice: increased locomotor activity and reduced stereotypic behavior [125]	→	3 [4]	within a human cohort-based clinical psychiatric study, increased stress resilience [126]	\rightarrow
63 DRD5		in models of human behavior using rats, Drd5-antagonist (rather Drd5- agonist) blocks freezing behavior in conditioned fear [127]	→	10 [4]	in models of human diseases using rats, prenatal nicotine exposure rises Drd5 level in the striatum as a cause of newborn mental disorders [128]	←
64 ESR2	2 [3]	within model of human disease using rats, ESR2-deficiency in adolescents reduces sperm quality in adults [129]	-		within model of human disease using rats, ESR2-excess in adolescents reduces sperm quality in adults [129]	←
65 F2		α1-antitrypsin inhibits F2 and, thereby, prevents thromboembolism and micro- and macrothrombosis in order to relieve COVID-19 [130]	→	2 [3]	increased risks of preeclampsia as one of the most challenging problems of modern obstetrics [131]	←
66 F3	2 [3]	ozone therapy suppresses F3 and, thereby, prevents thrombotic ischemic	→	5 [3]	increased risks of stroke and myocardial infarction as two most often causes of human death [133]	\leftarrow
67 F7	2 [3]	increased risks of episodic spontaneous difficult to stop life-threatening bleeding [134] ←	-	5 [3]	recombinant activated F7 is a life-saving drug for obstetric life-threatening bleeding [135]	\rightarrow
68 F8		hemophilia A: spontaneous hemorrhages in the brain, joints, muscles, internal organs and, as a result, disability [136]	_	1 [3]	increased risks of thrombosis provoking stroke and myocardial infarction as the two most frequent causes of death in humans [137]	←
69 F9	1 [3]	hemophilia B: spontaneous hemorrhages in the brain, joints, muscles, internal organs and, as a result, disability [138]	-	1 [3]	increased risks of myocardial fibrosis causing tachyarrhythmias, disability <i>via</i> heart failure and, ultimately, cardiovascular death [139]	←
70 F11	1 [3]	coagulation factor XI insufficiency provoking spontaneous bleeding and, ultimately, disability [140] ←	_	5 [3]	increased risks of angioedema provoking hypercapnic coma in case of carbon dioxide poisoning and, as a result, death [141]	←
71 FGF1	6 [4]	within a retrospective review of publications on wound healing in rats and mice as human disease models, delayed skin wound healing [142]	-	5 [4]	in human disease models using mice with artificial skin wounds treated with bacterial plasmid carrying FGF1 gene, improved wound healing [143]	\rightarrow
72 FGF3		within a model of human cord brain injury using zebrafish, inhibited formation of so-called "glial bridge" and prevented axon regeneration [144]	_	1 [4]	within a model of human cord brain injury using zebrafish, improved post- traumatic neuron regeneration [144]	\rightarrow
73 FGF4		within human disease models in vitro, miR-511 inhibits breast cancer proliferation and metastasis by down-regulating FGF4 expression [145]	→	2 [4]	within a model of human diseases using mice with artificial brain injury, improved post-traumatic neural tissue survival [146]	\rightarrow
74 FGF5	1 [4]	in human cancer models <i>in vitro</i> using non-small cell lung cancer cells,	→	1 [4]	in human disease models using mice treated with intranasal <i>Aspergillus fumigatis</i> , tissue remodeling as complications of chronic inflammation [148]	→
75 FGF6	2 [4]	in human disease models using mice at artificial injury treated with clodronate-containing liposomes, worsen skeletal muscle regeneration [149]	_	1 [4]	in human disease models using mice treated with intranasal <i>Aspergillus fumigatis</i> , tissue remodeling as complications of chronic inflammation [148]	→
76 FGF8	2 [4]	within a model of human diseases using Fgf8-deficient mice, increased risks of stress-induced anxiety-like behavior [149]	_	4 [4]	in human disease models using transgenic mice carrying Fgf8 under mouse mammary tumor virus promoter, increased risks of breast cancer [150]	² ←

<u>*Genes*</u>: DRD2, DRD3, DRD4, and DRD5, dopamine receptors D2, D3, D4, and D5, respectively; *ESR2*, estrogen receptor 2 (β); *F2*, *F3*, *F7*, *F8*, *F9*, and *F11*, coagulation factors II (synonym: thrombin), III (synonyms: thromboplastin, tissue factor), VII (synonym: proconvertin), VIII (synonym: hemophilia A), IX (synonym: hemophilia B), and XI, respectively; *FGF1*, *FGF3*, *FGF4*, *FGF5*, *FGF6*, and *FGF8*, fibroblast growth factors 1, 3, 4, 5, 6, and 8, respectively.

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[#] Gene	NSNP	Effect on reproductive potential [Reference]	ďŶ	Nsn	Effect on reproductive potential [Reference]	q.ð
77 FGF9	1 [4]	in human disease models using young and aged mice carrying artificial skin injury, worsen post-traumatic wound healing [151]	←		in human male infertility models using adult male mice whos testis were injected with lentivirus carrying <i>Fgf</i> 9, arrested spermatogenesis [152]	~
78 FGF10		in human newborn model using Fgf10-null mice, a congenital duodenum obstruction that needs surgery in just the 1st day of life [153]	←	2 [4]	0, 0 0 , 0	\rightarrow
79 FGF11	1 [4]	in human embryogenesis models using mice embryo carrying siRNA- caused Fgf11-knockdown, hampered forelimb bud development [154]	←	1 [4]	0 0	\rightarrow
80 FGF12	3 [4]	in human embryogenesis models using rats, slowed increase in aversive behavior from generation to generation as response to prenatal stress [156]	\rightarrow	5 [4]	within a human subfertile female cohort-based clinical study, raised	←
81 FGF13	3 [4]	within a model of human diseases using FGgf13-knockout mice, increased risks of both obesity and inability to keep core temperature [158]	←	4 [4]	0 50	\rightarrow
82 FGF14		in human disease models using in vivo FGF14-knockdown in adult Purkinje neurons, worsen motor activity, coordination and balance [160]	←	12 [4]		\rightarrow
83 FGF17	1 [4]	in human behavior models using Fgf17-deficient mice, reduced social contacts within opposite-sex pairs to explore a novel environment [171]	←	2 [4]		←
84 FGF18	1 [4]	within a model of human newborn using mice carrying a germline Fgf18- knockdown: died shortly after birth [173]	←		in human behavior models using Fgf18-infusion into mice with cerebral ischemia: better cerebral blood flow, memory and motor abilities [174]	\rightarrow
85 FGF19		within a human cohort-based clinical study, increased risks of coronary artery disease, which severity raises with FGF19-deficit raising [175]	←	1 [4]	5	
86 FGF20	1 [4]	within a model of human health models using Fgf20-deficient mice, impaired mammary gland morphogenesis during puberty [177]	←	9 [4]		
87 FGF21		within a model of human health using muscle-specific Fgf21-null mice, reduced risks of muscle loss and weakness during fasting [179]	\rightarrow	2 [4]		$^{2} \rightarrow$
88 FGF22		within a cohort-based clinical patient study, increased risks of depression [181]	←	4 [4]		¹ →
89 FGFR1	3 [4]	within a model of human embryogenesis using Fgfr1-null mice, where embryos displayed early growth defects and, eventually, lethality [182]	←	10 [4]		\rightarrow
90 FGFR2	10 [4]	within a model of women firtility using defective Fgfr1-mutant female mice, increased risks of both subfertility and pregnancy loss [184]	←	11 [4]		←
91 FGFR3		within a model of human diseases using mice carrying fibroblast-specific Fgfr3-knockdown, attenuated experimental skin fibrosis [186]	\rightarrow	8 [4]	0 1	_ ←
92 FGFR4	4 [4]	in human disease models using adult Fgfr4-null mice: increased risks of airway inflammation, bronchial obstruction, and right ventricular hypertrophy [188]	←	1 [4]	within a cohort-based clinical facioscapulohumeral muscular dystrophy	· _
93FGFRL1	3 [4]	in human embryogenesis models using Fgfrl1-knockout mice, newborn lethality through malformed diaphragm & lack metanephric kidneys [190]	←	6 [4]	within a model of lung cancer using a qPCR-based comparison between	\rightarrow
94 FLT1	3 [4]	within a cohort-based clinical study, reduced risks of preeclampsia as one of the main causes of maternal and neonatal mortality in the world [192]	\rightarrow	3 [4]	within a cohort-based clinical study, increased risks of preeclampsia as one	←

Genes: FGF9, FGF10, FGF11, FGF12, FGF13, FGF14, FGF17, FGF18, FGF19, FGF20, FGF21, and FGF22, fibroblast growth factors 9, 10, 11, 12, 13, 14, 17, 18, 19, 20, 21, and 22, respectively; FGFR1, FGFR2, FGFR3, and FGFR4, fibroblast growth factor receptors 1, 2, 3, and 4, respectively; FGFR1, fibroblast growth factor receptor like protein 1; FLT1, Fms-related receptor tyrosine kinase 1,.

	Human		Deficit (↓)			Excess (↑)	_
#	Gene	Nsnp	Effect on reproductive potential [Reference]	ď₽	Nsnp	Effect on reproductive potential [Reference]	₹₽
95	FLT4	2 [4]	FLT4-blockade suppresses metastasis of melanoma cells by impaired lymphatic vessels [193]	\rightarrow	11 [4] inc	creased risks of inflammatory neovascularization after injury [194] •	<u> </u>
96	FLT3LG	2 [4]	within a model of human diseases using Flt2lg-knockout mice: reduced severity of artificial hepatic ischemia/reperfusion injury [195]	\rightarrow		in human disease models using artificially burn-injured mice with injection of recombinant FLT3LG, resistant to wound infections [196]	\rightarrow
97	FOS	4 [2]	in human obesity model using mice hypothalamic cells, Fos-inhibitor T-5224 regains gonadotropin-releasing hormone level as fertility [197]	\rightarrow	8 [2]	improved maturation of oocytes [198]	→
98	GABARAP	1 [4]	within a model of human diseases using adult male rats, reduced both fear- potentiated startle and fear-memory [199]	\rightarrow	3 [4]	within a model of human diseases using HEK293 cells, hypersensitivity to pain caused by physical stimuli [200]	i—
990	GABARAPL1	9 [4]	in human disease models using rats with low-protein diet during pregnancy and lactation, higher risks of arterial hypertension in adult offsprings [201]	←	10 [4]	within a model of human health using mice performing a low- intensity running exercise, reduced muscle endurance [202]	<u> </u>
100	GABARA PL2	4 [4]	retarded both neutrophilic differentiation and wound healing [203]	←	10 in [4]	mproved autophagy within odontogenic differentiation of dental pulp cells during healing a tooth injury [204]	→
101	GABBR1	1 [4]	within a cohort-based clinical study, incresed risks of schizophrenia, bipolar disorder, and major depression [205]	←		human disease models using transgenic mice injected with pCI-vector Promega) carrying Gabbr1, reduced pathological pain sensitivity [206]	\rightarrow
102	GABBR2	1 [4]	within a cohort-based clinical study, incresed risks of schizophrenia, bipolar disorder, and major depression [205]	←	[4] lab	in human disease models using mice with artificial injury of vestibular byrinth and Gabbr2-agonist: accelerated repair of gait and reflexes [207]	\rightarrow
103	GABRA1	4 [4]	in human disease models using pregnant mice injected with valproic acid as autism spectrum disorder inductor: social disorders in offsprings [208]	←	4 in l [4] GA	human disease models using mutant mice Gabba1:270S>H increasing ABA-sensitivity: less body size, motor coordination and viability [209]	<u></u>
104	GABRA2	5 [4]	in human disease models using mice with artificial sciatic nerve injury treated, where Gabra2-antisence worsens pain hypersensitivity [210]	←		human behavior models using chronic social defeat stress in male mice, increased risks of mixed anxiety/depression-like state [211]	
105	GABRA5	2 [4]	in human behavior models using rats infused with chloroform, increased risks of both memory impairment and learned helplessness [212]	←		vithin a model of human neuropsychiatric and neurodevelopmental sorders using mutant mice, higher risk of anxiety-like behavior [213]	<u></u>
106	GABRA6	1 [4]	in human pregnancy models using vitamin C-deficient pregnant mice supplemented with vitamin C (norm) and without it: higher risk of stillbirths [214]	←		a cohort-based clinical study of SNPs within miRNAs, norm of hich represses GABRA6, associated them with panic disorder [215]	-
107	GABRB1	2 [4]	within a retrospective review of many cohort-based clinical studies, increased risks of epilepsy, autism, bipolar disorder and schizophrenia [216]	←		nly simultaneous silencing of gabrb1 expression and gabrb1-protein inhibition lows the prion protein level in neuroblastoma cells [217]	<u></u>
108	GABRB2	3 [4]	in human disease models using pregnant mice injected with valproic acid as autism spectrum disorder inductor: social disorders in offsprings [208]	←		human pregnancy models using rats with artificial flurothyl-induced neonatal recurrent seizures: accelerated developing brain injury [218]	<u> </u>
109	GABRB3	5 [4]	within a model of human embryogenesis using Gabrb3-knockout mice, increased risks of either newborn lethality or reduced life span [219]	←		human disease models using pregnant mice at ethanol diet, higher risk of utism-like asocial behavior and memory deficits in male offsprings [220]	<u> </u>
110	GABRD		within a cohort-based clinical spermatozoa-related study, increased risks of male infertility [221]	←		ithin a model of human activity-based anorexia using adolescent mice, gher risk of stress-caused anxiety and weight loss in adolescence [222]	<u> </u>
111	GABRE	2 [4]	in human pregnancy model using female rats administered with Gabre- agonist, increased risks of life-threatening respiratory rhythm disorder [223]	←		rithin a model of human pentobarbital side effects using rat neurons transfected with adenovirus carrying Gabre, cardioprotection [224]	\rightarrow

<u>*Genes:*</u> *FLT4*, Fms-related receptor tyrosine kinase 4; *FLT3LG*, Fms-related receptor tyrosine kinase 3 ligand; *FOS*, AP-1 transcription factor subunit Fos proto-oncogene; *GABARAP*, gammaaminobutyric acid type A (GABA(A)) receptor-associated protein; *GABARAPL1* and *GABARAPL2*, GABA(A) receptor-associated protein like proteins 1 and 2, respectively; *GABBR1* and *GABBR2*, GABA(B) receptor subunits 1 and 2, respectively; *GABRA1*, *GABRA2*, *GABRA5*, and *GABRA6*, GABA(A) receptor subunits $\alpha 1$, $\alpha 2$, $\alpha 5$, and $\alpha 6$, respectively; *GABRB1*, *GABRB2*, *GABRB3*, *GABRD*, and *GABRE*, GABA(A) receptor subunits $\beta 1$, $\beta 2$, $\beta 3$, δ , and ε , respectively.

	Human		Deficit (↓)		Excess (↑)
#	Gene	Nsnp	Effect on reproductive potential [Reference] o	Ŷ	V _{SNP} Effect on reproductive potential [Reference] dQ
112	GABRG1		in human disease models using sodium-butyrate treated mice administered with Gabg1-agonist, higher risk of asocial autism-like behavior [225]		1within a model of human disease using sodium-butyrate treated[4]mice, improved social behavior [225]
113	GABRG2	2 [4]	within a model of human diseases using Gabrg2-knockout mice, increased risks of asocial depressive behavior [226]	_	 1 within a model of human diseases using male mice stressed in infant [4] age, increased risks of anxiety-like asocial behavior in adult age [227]
114	GABRG3	3 [4]	within a model of human diseases using mice carrying natural Gabrg3- deletion, higher risk of both Angelman's and Prader-Willi's syndromes ← [228]	_	 9 in human disease models using artificial temporal hearing loss in rats, [4] increased risks of hyperacusis up to asocial depressive behavior [229]
115	GABRP	3 [4]	within a cohort-based clinical study of cervical cancer women overexpressing _ microRNA-320c targeting GABRP, reduced risks of metastasis [230]		 within a metastatic xenograft mouse model using human ovarian (4) carcinoma SK-OV-3 cells, increased risks of metastasis [231]
116	GABRR1		within a model of human behavior using Gabrr1-knockout mice, increased risks of mechanical pain hypersensitivity [232]	_	 in human health models using CD34+ cells treated with GABRR1 agonists: improved megakaryocyte colonies as sources for platelet in blood [233]
117	GABRR2	1 [4]	within a model of human diseases using rats studied with polyclonal	→	within a model of human pregnancy using pregnant rats: improved "maternal brain" development and, thus, "maternal behavior" [235] \rightarrow
118	GABRR3	2 [4]	within a cohort-based clinical human blood samples study, worsen healing of wounds owing to accelerated platelet senescence [236]		 2 in human disease models using mice treated with polyinosinic- [4] polycytidylic acid, hypersusceptibility to excitotoxic brain insult [237]
119	GCG	2 [3]	reduced pregnancy rate [238] ←	_	reduced pregnancy rate [239] ←
120	GDNF	1 [4]	within a model of human spermatogenesis using mice: hindered spermatogonial stem cells self-renewal and impaired fertility [240]	_	 in human spermatogenesis models using mice spermatogonial progenitor [4] cells and GDNF: improved proliferation of these cells & male fertility [241]
121	GFRA1	2 [4]	in human spermatogenesis models using adult male rats treated with pyrethroids: impaired sperm production and development[242]	_	 in human spermatogenesis models using mice pup spermatogonial progenitor cells treated with diethylstilbestrol: testicular cancer in adult [243]
122	GFRA2		within a model of human diseases using Gfra2-knockout mice, impaired gastrointestinal transit rate [244]	_	 within human disease models using mice, improved post-injury survival of all motoneurons except oculomotor and abducens nerves [245]
123	GFRA3	1 [4]	increased risks of somatosensory system neurodegeneration [246] ←	_	improved neural regeneration after injury [247] \rightarrow
124	GFRA4	3 [4]	within a model of human diseases using GFRA4-knockout mice, calcitonin deficit rises prematurely bone formation rate in adolescent [248]	_	$ \begin{array}{c} 2 \\ [4] \end{array} \text{improved neuronal survival and neurite outgrowth [249]} \rightarrow \end{array} $
125	GH1	2 [3]	increased mortality from cardiovascular disease [250] ←	_	2somatotropin is used as a drug to prolong[3]the reproductive age in women [251]
126	GJA5	3 [3]	increased risks of the heart morphogenesis disorders, which result in arrhythmias and cardiovascular diseases [252]	_	increased arteriogenesis as the human body response to a low oxygen \rightarrow level at chronic hypoxia [253]
127	GMFB	2 [4]	within a model of human diseases using Gmfb-knockout mice, reduced	→	in human disease models using male mice with artificial brain injury: \leftarrow increased risks of lung injury as a complication of brain injury [255]
128	GMFG	2 [4]	within a model of human muscle ischemic injury complications using human cardiomyocyte cells, increased risks of necrosis [256]	_	 4 in women fertility models using both granulosa and theca cells from [4] antral bovine follicles, improved ovarian functions [257]

<u>*Genes:</u></u>, <i>GABRG1, GABRG2, GABRG3, GABRP, GABRR1, GABRR2,* and *GABRR3,* GABA(A) receptor subunits γ 1, γ 2, γ 3, π , ϱ 1, ϱ 2, and ϱ 3, respectively; *GCG,* glucagon; *GDNF,* glial cell derived neurotrophic factor; *GFRA1, GFRA2, GFRA3,* and *GFRA4,* glial cell line-derived neurotrophic factor receptor α 1, α 2, α 3, and α 4, respectively; *GH1,* growth hormone 1 (synonym: somatotropin); *GJA5,* connexin 40 (synonym: gap junction protein α 5); *GMFB* and *GMFG,*, glia maturation factor β and γ , respectively.</u>

	Human		Deficit (↓)		Excess (↑)		
#	Gene	NSNP	Effect on reproductive potential [Reference]	ď₽	Nsnp	Effect on reproductive potential [Reference]	Ъ₽
129	GPR18	2 [4]	in human disease models using rats with artificial ischemic stroke administered with GPR18-antagonist, worsen post-injury repair [258]	←	1 [4]	in human disease models using rats with artificial injury treated with N-arachidonoyl-serotonin, increased pain sensitivity threshold [259]	\rightarrow
130	GPR55	1 [4]	within a model of women infertility using female mice administered with GPR55-antagonist, impaired oocyte maturation [260]	←	4 [4]	in human disease models using rats with intravenous administration of GPR55-receptor agonist, reduced pain-related behavior [261]	\rightarrow
131	GPR119	2 [4]	within a model of human diseases using Gpr119-knockout mice: resistant to hypophagia due to normalized gut hormone levels and food intake [262]	\rightarrow	2 [4]	in human obesity models using high-fat-fed rats with oral administration of GPR119-agonist: reduced both food intake and body weight gain [263]	\rightarrow
132	GRIA1	2 [4]	within a retrospective clinical cohort-based transcriptome meta-analysis, increased risks of polycystic ovary syndrome [264]	←	3 [4]	in human behavior models using pregnant rats at a high-caloric palatable diet, increased risks of anxiety in male offsprings [265]	←
133	GRIA2	7 [4]	within a model of human behavior models using Gria2-knockout mice: impaired stimulus-reward learning with conditioned stimuli[266]	←	10 [4]	within a retrospective clinical cohort-based transcriptome meta- analysis, increased risks of uterine leiomyomas and infertility [267]	←
134	GRIA4	2 [4]	within a model of human behavior using Gria4-knockout mice, improved spatial working memory and reduced fright behavior [268]	\rightarrow	6 [4]	within a clinical cohort-based transcriptome of postmortem subjects, increased risks of major depressive disorder up to suicide [269]	←
135	GRIK1	1 [4]	within a model of human behavior using Grik1-knockout mice: reduced sensitivity to itching and scratch pain that improves wound healing [270]	\rightarrow	5 [4]	within a model of human behavior using mice treated with pharmacological Grik1-activation: pain hypersensitivity [271]	\leftarrow
136	GRIK2	6 [4]	based on a case of father carrying a GRIK2-damage: increased risks of stillbirth, miscarriage, as well as son severe intellectual disability [272]	←	3 [4]	in human behavior model using rats injected with formalin into rectum mucosa: hypersensitivity to acute inflammatory pain [273]	←
137	GRIK3		based on a case of girl carrying a GRIK3-damage: increased risks severe developmental delay affecting language and fine motor skills [274]	←	1 [4]	within a clinical cohort-based transcriptome of postmortem subjects, increased risks suicide in major depressive disorder [269]	\leftarrow
138	GRIK5	1 [4]	within a model of human aging using mice administered with D- galactose in order to induce aging artificially: delayed aging [275]	\rightarrow	3 [4]	according to a pharmaceuticals report, γ-aminobutyric acid treats bipolar disorder through an GRIK5-upregulation [276]	←
139	GRIN1	1 [4]	within a model of human pregnancy using pregnancy rats under artificial hypoxia, impaired learning and memory ability in adolescent offspring [277]	←	8 [4]	in human behavior models using pregnant rats at a high-caloric palatable diet, increased risks of anxiety in male offspring [265]	\leftarrow
140	GRIN2A	2 [4]	in human behavior models using mice under scream sound stress during 21 postnatal days, impaired spatial learning and memory in adult males [278]	←	2 [4]	in human behavior models using transgene mice overexpressing Grin2a in neurons, improved long-term fear memory [279]	←
141	GRIN2C	2 [4]	in human pregnancy models using pregnant mice with voluntary alcohol drinking, anxiety and learning deficits in adolescent male offspring [280]	←		within a model of human disease using mice infused with Grin2C- agonists, improved motor function [281]	\rightarrow
142	GRIN2D		within a model of human behavior using Grin2d-knockout male mice: exacerbated negative emotional behavior [282]	←	4 [4]	within a model of human disease using rats with artificial pulpitis with bacterial infection, neuropathic pain hypersensitivity [283]	←
143	GRIN3A		in a model of human drug addiction using Grin3a-knockout mice, no cocaine-caused long-term burst firing of dopamine neurons [284]	\rightarrow	1 [4]	increased risks of inattentive behavior [285]	\leftarrow
144	GRIN3B		within a model of human behavior using Grin3b-knockout mice: significant impairment in motor learning or coordination [286]	←	4 [4]	in human behavior models using norm <i>versus</i> Grin3b-knockout mice: improved motor learning or coordination and reduced anxiety [286]	←
145	GRINA	3 [4]	within a clinical cohort-based pharmacological study, topiramate as a drug reduces drug addiction through GRINA-downregulation [287]	~	8 [4]	within a clinical cohort-based postmortem study, increased risks of major depressive disorder [288]	←

<u>Genes</u>: GPR18, GPR55, and GPR119, G protein-coupled receptors 18, 55, and 119, respectively; GRIA1, GRIA2, and GRIA4, glutamate ionotropic receptor AMPA type subunits 1, 2, and 4, respectively; GRIK1, GRIK2, GRIK3, and GRIK5, glutamate ionotropic receptor kainate type subunits 1, 2, 3, and 5, respectively; GRIN1, GRIN2A, GRIN2C, GRIN2D, GRIN3A and GRIN3B, glutamate ionotropic receptor NMDA type subunits 1, 2A, 2C 2D, 3A, and 3B; GRINA, glutamate ionotropic receptor NMDA type subunit associated protein 1.

	Human		Deficit (↓)			Excess (↑)	
#	Gene	Nsnp	Effect on reproductive potential [Reference]	ď₽	Nsni	P Effect on reproductive potential [Reference]	₽D
146	GRM1		within a pharmacological clinical study, isoflurane as a drug protects the myocardium against ischemia and injury by upregulating GRM1 [289]	←	4 [4]	within a clinical cohort-based transcriptome of postmortem subjects, increased risks of major depressive disorder up to suicide [269]	←
147	GRM2	1 [4]	within a model of human behavior using rats microinjected with GRM2- antagonist: increased risks of fearful motivation in form of burying [290]	←	1 [4]	within a model of human diseases using human sensory neurons from donors without a history of chronic pain: reduced pain sensitivity [291]	
148	GRM3	1 [4]	within a model of human behavior using Grm3-knockout mice: increased risks of schizophrenia-like hyperactive asocial aggressive behavior [292]	←	3 [4]	within a model of human behavior using normal mice administered with selective negative allosteric Grm3-modulator: worsen learning [293]	$^{1} \rightarrow$
149	GRM4	2 [4]	weakened microglial inflammation during post-injury brain repair [294]	\rightarrow	5 [4]	increased risks of depression-like behavior [295]	←
150	GRM5	2 [4]	in human behavior models using mice administered with Grm5- antagonist: reduced pain sensitivity [296]	\rightarrow	3 [4]	in human behavior models using pregnant rats exposed to repeated episodes of restraint stress: reduced stress resilient in adult offspring [297]	←
151	GRM7	3 [4]	within a model of men subfertility using adult male Grm7-knockout mice: subfertility, lowed insemination capability, excess defective spermatozoa [298]	←	6 [4]	in human embryo models using <i>Grm7</i> -knockdown pregnant mice injected with plasmid carrying <i>Grm7</i> into fetal brain: ameliorated neurogenesis defects [299]	
152	GRM8	4 [4]	within a model of human behavior using Grm8-deficient mice: dramatic reduction in contextual fear [300]	\rightarrow	5 [4]	in human behavior models using rats exposed with artificial injury and Grm8-agonist microinjection into brain: reduced pain sensitivity [301]	←
153	GSTM3	2 [3]	increased risk of non-obstructive azoospermia [302]	←	2 [3]	within human diseases model using cows, increased frequency of natural fertilization compared to artificial fertilization [303]	\rightarrow
154	GTPBP6	3 [5]	increased intelligence quotient IQ scores in men [304] that is negatively significantly associated with amount of their siblings and cousins [305]	←	3 [5]	reduced intelligence quotient IQ scores in men [304] that is positively significantly associated with amount of their siblings and cousins [305]	\rightarrow
155	HBB	9 [3]	thalassemia impairs women's reproductive health [306]	←		within traditional Chinese medicine, Jian-Pi-Yi-Sheng decoction (JPYS) rises hemoglobin to treat anemia in chronic kidney diseases [307]	\rightarrow
156	HBD	2 [3]	thalassemia impairs women's reproductive health [306]	←		within code for hemoglobin subunits α , β [307]	\rightarrow
157	HBG2	1 [3]	thalassemia impairs women's reproductive health [306]	←		within traditional Chinese medicine, Jian-Pi-Yi-Sheng decoction (JPYS) rises hemoglobin to treat anemia in chronic kidney diseases [307]	\rightarrow
158	HSD17B1	3 [3]	increased risk of breast cancer [308]	←	1 [3]	increased risk of breast cancer [309]	←
159	HTR1A	1 [4]	within a model human behavior using Htr1a-knockout mice: increased risks of anxiety-like behavior [310]	←	1 [4]	in human behavior models using chicken embryos exposured with corticosterone during incubation: aggressiveness in chicks [311]	\rightarrow
160	HTR1B		within a model human behavior using Htr1b-knockout mice: increased risks of aggressive behavior [312]	\rightarrow	3 [4]	within human behavior models using transgene mice infected with viral vector carrying Htr1b: increased risks of stress-induced anxiety [313]	¹ ←
161	HTR1F	1 [4]	in human milk feeding baby models using dairy calves fed with milk and serotonin precursor: better serotonergic regulation of energy metabolism [313]	\rightarrow		within a model human behavior using rats injected with formalin and, next, administered Htr1f-agonist: reduced inflammatory pain [314]	←
162	HTR2A	1 [4]	within a model human disease using adipose tissue-specific Htr2a- knockout mice: resistance to obesity during high-fat diet [315]	\rightarrow		within a clinical cohort-based study, increased risks of hypertrophic hearts as the leading cause of sudden death in young athletes [316]	←

Genes: *GRM1*, *GRM2*, *GRM3*, *GRM4*, *GRM5*, *GRM7*, and *GRM8*, glutamate metabotropic receptors 1, 2, 3, 4, 5, 7, and 8, respectively; *GSTM3*, glutathione S-transferase μ3; *GTPBP6*, GTP-binding protein 6; *HBB*, *HBD*, and *HBG2*, hemoglobin subunits β, δ, and γ2, respectively; *HSD17B1*, hydroxysteroid 17β dehydrogenase 1; *HTR1A*, *HTR1B*, *HTR1F*, and *HTR2A*, 5-hydroxytryptamine receptor 1A., 1B, 1F, and 2A, respectively.

" Human		Deficit (↓)		Excess (↑)	
[#] Gene	NSNP	Effect on reproductive potential [Reference] of	Nsn	P Effect on reproductive potential [Reference]	ďŶ
163 HTR2C		in human health models using neuroblastoma cells treated with psychoactive drugs at environmental levels: higher risk of autism spectrum disorders [317]	1 [4]	within a model human behavior using tame and aggressive rats bred artificially, inhibited fear-evoked aggressive behavior [318]	\leftarrow
164 HTR3A	3 [4]	increased risks of sudden cardiac death during pregnancy [319] \leftarrow		within a model of human health using mice, improved hippocampal neurogenesis and antidepressant effects caused by physical exercise [320]	\rightarrow
165 HTR3B	1 [4]	within a model of human's both 'anger-in' and 'anger-out' emotions using rats, decreased risks of anger-related resolute behavior [321]		reduced risks of pulmonary embolism, severe cases of which can lead to passing out, abnormally low blood pressure, and sudden death [322]	\rightarrow
166 HTR3C	1 [4]	within a model of human diseases using HEK293 cell line treated with antibody against HTR3C: enhanced aggressive behavior [323] \rightarrow	2 [4]	within a model of human diseases using HEK293 cell line treated with antibody against HTR3C: reduced aggressive behavior [323]	←
167 HTR3D	1 [4]	within a model of human diseases using HEK293 cell line treated with antibody against HTR3D: reduced aggressive behavior [323]	2 [4]	within a model of human diseases using HEK293 cell line treated with antibody against HTR3D: enhanced aggressive behavior [323]	\rightarrow
168 HTR3E	4 [4]	within a model of human diseases using HEK293 cell line treated with antibody against HTR3E: reduced aggressive behavior [323]	1 [4]	within a model of human diseases using HEK293 cell line treated with antibody against HTR3E: enhanced aggressive behavior [323]	\rightarrow
169 HTR4	2 [4]	within a model of human behavior using mice, increased risks of depression, anxiety and affective disorders [324]	13 [4]	within a model of human newborns using neonatal calves, improved development of the immune system and gastrointestinal tract [325]	\rightarrow
170 HTR5A		within a model of human newborns using pregnant Brahman cows under stress, elevated temperament scores in male offspring [326] →	1 [4]	within a clinical cohort-based pregnant women study, increased risks of fetal growth restriction [327]	←
171 HTR7		within a clinical cohort-based irritable bowel syndrome study, visceral abdominal pain hypersensitivity up to sexual disfunction [328]	1 [4]	in human lactogenesis models using pregnant rats under high-fat diet, delayed lactogenesis onset leading to mammary gland inflammation [329]	←
172 IGF1	2 [4]	within a model of women fertility using Holstein Friesian cows, imbalanced transition from pregnancy to lactation up to subfertility in future [330]		within a model of women fertility using female rats injected with human amnion epithelial cells in uterine, increase pregnancy rate [331]	\rightarrow
173 IGF2	2 [4]	within bioinformatics retrospective meta-analysis of the public biomedical databases, higher risk of diminished ovarian reserve up to subfertility [332]	1 [4]	in women fertility models using IGF2 supplementation in oocyte cultures from aged female mice, improved oocyte developmental competence [333]	\rightarrow
174 IGF1R	5 [4]	within a model of human embryogenesis using blastocysts from female rabbites with artificially induced type 1 diabetes: subfertility [334]	5 [4]	within a model of human embryogenesis using mice embryos under hypoxia: improved symmetric division during embryogenesis [335]	\rightarrow
175 IL1B	1 [3]	reduced risks of bone marrow hyperplasia and bone deformation in case of \rightarrow bacterial invasion [336]	1 [3]	increased circadian hypersensitivity to pain [337]	←
176 IL3RA	2 [5]	within a human cancer model using acute myeloid leukemia cells, SS30 thioaptamer inhibites IL3RA that increases survival [338] \rightarrow	3 [5]	increased risks of acute myeloid leukemia in children [339]	←
177 IL6	3 [4]	in human "mother-offspring" relationship models using pregnant pigs under alfalfa meal diet reducing IL6 level: more fertility and offspring survival [340] \rightarrow	3 [4]	in women reproductive ageing models using immune cell populations from mice ovaries: accelerated decline in follicle number and oocyte quality [341]	
178 IL6R	5 [4]	within a model of human diseases using transgenic mice under bacterial infection: reduced risks of tumorigenesis in chronic inflammation [342] \rightarrow	5 [4]	within a clinical cohort-based study using peritoneal fluid from patients with versus without endometriosis, higher risk of endometriosis [343]	←
179 IL6ST	7 [4]	in a model of human diseases using mice, exacerbated inflammatory responses that is eventually, increased mortality during sepsis [344] \leftarrow	8 [4]	increases sensitivity to fatigue during submaximal exercise in sedentary middle-aged men (i.e., reproductive age men) [345]	~

<u>Genes</u>: HTR2C, HTR3A, HTR3B, HTR3C, HTR3D, HTR3E, HTR4, HTR5A, and HTR7, 5-hydroxytryptamine receptors 2C, 3A, 3B, 3C, 3D, 3E, 4, 5A, and 7, respectively; *IGF1* and *IGF2*, insulin-like growth factors 1 and 2, respectively (synonyms: somatomedin C and preptin, respectively); *IGF1R*, insulin like growth factor 1 receptor; *IL1B*, interleukin 1β; *IL3RA*, interleukin 3 receptor subunit *α*; *IL6*, and *IL6R*, interleukin 6 (synonym: interferon β2) and its receptor, respectively; *IL6ST*, interleukin 6 signal transducer.

	Human		Deficit (↓)		Excess (↑)		
#	Gene	Nsni	Effect on reproductive potential [Reference]	ď₽	Nsnp	Effect on reproductive potential [Reference]	ď₽
180	IL9R	1 [5]	trophoblast implantation impaired within preeclampsia [346]	\leftarrow	1 [5]	increased risks of life-threatening anaphylactic shock [347]	~
181	IL11		in women fertility models using pregnant mice administered with IL11- blockator: reduced risks of pregnancy and preserved fertility in cancer [348]	\rightarrow	5 [4]	within a model of women fertility using transgenic female mice: enhanced decidualization [349]	\rightarrow
182	IL11RA		within a model of women fertility using Il11ra-knockout female mice: infertility through impaired decidualization [350]	←	7 [4]	within a model of human diseases using mice: increased risks of osteosarcoma [351]	←
183	IL27	1 [4]	within a clinical cohort-based study: increased risks of autoimmunity- related recurrent pregnancy loss [352]	←	1 [4]	within a clinical cohort-based study: increased risks of preterm birth through excessive inflammatory response in fetal membranes [353]	←
184	INS	1 [3]	within a model of human diseases using sheeps, hypoinsulinemia slows down fetal growth and development [354]	←	2 [3]	increased risks of neonatal diabetes mellitus, which can often progress to type I diabetes mellitus [355]	←
185	KDM5D	3 [5]	increased risks of aggressive prostate cancer [356]	←		increased risks of cardiovascular diseases [357]	←
186	LEP	1 [1]	increased risks of hypothalamic amenorrhea with dysfunction of hypothalamus endocrine axes and, ultimately, subfertility [358]	←	1 [1]	increased risks of subfertility as an obesity complication [359]	\leftarrow
187	LGI4		within a clinical cohort-based loss-of-functuion LGI4 family study: increased risks of arthrogryposis multiplex congenita [360]	\leftarrow	2 [2]	within a model of human behavior using tame and aggressive rats: increased risks of aggressive behavior [361]	\rightarrow
188	LIFR		within a clinical cohort-based infertile versus fertle women study: increased risks of infertility [360]	←	6 [4]	in human disease models using female rhesus macaque administered with soluble LIFR: increased risks of blocked ovulation [361]	←
189	MBL2	2 [3]	increased risks of recurrent late pregnancy losses at unclear etiology [362]	←	1 [3]	exogenous recombinant human MBL2 is used as a nonspecific immunomodulatory within adjuvant therapy against COVID-19 [363]	$_{]} \rightarrow$
190	MMP12	2 [3]	within models of human diseases using MMP12-knockout mice, low differentiation of oligodendrocytes of the central nervous system [364]	←		trophoblast implantation improved within pregnancy [365]	\rightarrow
191	MTHFR	2 [3]	increased risks of adverse pregnancy outcomes [366]	←	4 [3]	increased risks of preeclampsia as one of the most challenging problems of modern obstetrics [367]	←
192	NGFR		within a model of human embryogenesis using rat embryos: increased risks of fetal death [368]	←	3 [1]	in human disease models using newborn rats administered with estradiol valerate: increased risks of infertility in adul [369]	←
193	NLGN4Y	. 1 [5]	increased risks of both primary prostate cancer and its biochemically- induced recurrence [370]	←	2 [5]	increased risks of male infertility [371]	←
194	NOS2		in a model of human diseases using triple NOS1,2,3-knockout (because of their interchangeability) mice, reduced survival and fertility [372]	←	1 [3]	increased risks of diabetes mellitus in pregnancy, which is conventionally considered as pre-diabetes of both type I and II [374]	←
195	NPY	3 [4]	in a model of human health using Vgf-knockout mice, small size, low fat stores, hypermetabolism, hyperactivity, hypoleptinemia, infertility [375]	←	1 [4]	within a model of human obese using obese mice ob/ob line, rised risks of obesity, type 2 diabetes, and, eventually, subfertility [376]	←
196	NPY1R	7 [4]	within a model of human "mother-offspring" relationship using pregnant rats under high-fat diet embryos: increased risks of obesity in offspring [377]	←	5 [4]	within a model of human diseases using streptozotocin-induced type I diabetes in male rats: increased risks of type I diabetes [378]	÷ ←

<u>Genes</u>: IL9R, interleukin 9 receptor; IL11 and IL11RA, interleukin 11 and its receptor subunit *α*, respectively; IL27, interleukin 27; INS, insulin; KDM5D, lysine demethylase 5D; LEP, leptin; LG14, leucine-rich glioma-inactivated gene 4; LIFR, leukemia inhibitory factor receptor *α*; MBL2, mannose binding lectin 2; MMP12, matrix metallopeptidase 12 (synonym: macrophage elastase); MTHFR, methylenetetrahydrofolate reductase; NGFR, nerve growth factor receptor; NLGN4Y, neuroligin 4 Y-linked;; NOS2, nitric oxide synthase (inducible, hepatocytes, macrophage;); NPY, neuropeptide Y; NPY1R, neuropeptide Y receptors Y1.

" Human		Deficit (↓)	Excess (↑)				
[#] Gene	Nsnp	Effect on reproductive potential [Reference]	ď₽	Nsni	<i>p</i> Effect on reproductive potential [Reference] گ		
197 NPY2R		in human disease models using mice with artificial albuminuria treated with NPY2R-inhibitor: lesser risks of kidney failure and premature death [379]	\rightarrow	2 [4]	within a clinical cohort-based study: increased risks of depression-like behavior, which may be relieved due to antidepressants [380]		
198NPY4R		in human newborn models using newborn mice milk-fed with polychlorinated biphenyls at environmental levels: anxiety-like behavior in adulthood [381]	←	1 [4]	within a clinical cohort-based study on NPY4R copy number natural variation in-between 2 and 4: increased risks of obesity [382]		
199 NPY5R		within a model of human obesity using Npy5r-knockout mice at high-fat diet with anorectic agents: resistance to anorectic drugs in obesity [383]	←	5 [4]	within a model of human pregnancy using mid- and late-pregnant rats: \rightarrow improved maternal behavior [79]		
200 NR5A1		gender-specifically increased risks of gonadal dysgenesis in men [384]	←	4 [3]	gender-specifically improved sexual determination/differentiation, adrenal and gonadal development in men [385] \rightarrow		
201 NRG1	5 [4]	within a model of human embryogenesis using tissue-specific Nrg1- knockout male mice embryos: impaired testis development [386]	←	18 [4]	in human disease models using juvenile mice administered with exogenous NRG1: higher risk of schizophrenia neuropathology [387] \leftarrow		
202 NRG2	3 [4]	within a model of human behavior using Ng2-knockout mice: reduced anxiety-like behavior, hyperactivity and prepulse inhibition deficit [388]	\rightarrow	7 [4]	in human behavior models using high- and low-anxious male rats according to behavioral tests: higher risk of anxiety-like behavior [389]		
203 NRG3	3 [4]	within a model of human behavior using Nrg3-knockout mice: hyperactivity, impaired prepulse inhibition and fear deficiency [390]	\rightarrow	1 [4]	within a model of human spermatogenesis using mice testis fragments cultured with NRG3: improved spermatogonia proliferation [391] \rightarrow		
204 NRG4		within a model of human obesity using tissue-specific conditional Nrg4- knockout mice: vascular rarefaction within adipose tissue in obesity [392]	\rightarrow	2 [4]	within a clinical cohort-based women study: increased risks of obesity- related polycystic ovary syndrome up to subfertility [393]		
205 NRP1	12 [4]	within a model of women reproductive health using tissue-spesific Nrp1- knockdown mice: impaired ovariogenesis [394]	←	16 [4]	in human cancerogenesis models using human glioma cells exposed with synthetic NRP1-blocking peptides: retarded glioma growth [395] \leftarrow		
206 NRP2	3 [4]	in models of human diseases using NRP2-knockout bladder cancer cell lines, improved patient survival in antitumor radiochemotherapy [396]	\rightarrow	1 [4]	increased risks of post-traumatic vascular neointimal hyperplasia [397] \leftarrow		
207 NRTN	2 [4]	within a model of human diseases using Nrtn-knockout mice: the enteric nervous system defects (e.g., reduced gastrointestinal motility) [398]	←	1 [4]	in human behavior models using transgenic mice overexpressing Nrtn: behavioral hypersensitivity to environmental stimuli [399]		
208 NTF3	1 [4]	within a clinical cohort-based study: increased risks of depressive behavior [400]	←	3 [4]	in human disease models using mice with artificial multiple sclerosis treated with full-term human placenta: Ntf3 excess biomarks this disease relief [401] \rightarrow		
209 NTF4		within a clinical cohort-based post-mortem brain study: increased risks of cognitive impairment [402]	←	2 [4]	in human "mother-offspring" relationship models using pregnant rats of low and high physical activity: improved learning and memory in offspring [403] \rightarrow		
210NTRK1	1 [4]	within a clinical cohort-based study of women with silent NTRK1 gene versus norm: increased risks of external genital endometriosis [404]	←	1 [4]	in human pain sensitivity models using mice with artificially induced mechanical pain: reduced neuropathic allodynia [405]		
211NTRK2		within a model of women reproductive health using mutant Ntrk2-deficient female mice: post-pubertal oocyte death and early adulthood infertility [406]	←	4 [4]	in human "mother-offspring" relationship models using pregnant rats of low & high \rightarrow physical activity: tendency to improve learning & memory in offspring [403]		
212 NTRK3	3 [4]	in human diseases models using Ntrk3-knockout and Ntrk3-excessive mice: loss of kidney podocytes that accelerates aging through glomerular disease [407]	\leftarrow	19 [4]			
213 OGFR	1 [4]	within a clinical case report on human male newborn carrying loss-of-function mutation within OGFR gene: lifelong inflammation of skin, bowel, & lungs [409]	\leftarrow	4 [4]	within a model of human diseases using transgenic mice overexpressing Ogfr: impaired wound healing [410]		
214 OPRD1		within a model of human behavior using Oprd1-knockout mice: increased risks of both anxiogenic- and depressive-like behavior [411]	←	1 [4]	in human men subfertility model using mice sperm incubated with OPRD1- agonist: reduced both fertilization rate and number of reached blastocysts [412] \leftarrow		

<u>Genes</u>: NPY2R, NPY4R, and NPY5R, neuropeptide Y receptors Y2, Y4, and Y5, respectively; NR5A1, steroidogenic factor 1; NRG1, NRG2, NRG3, and NRG4, neuregulins 1, 2, 3, and 4, respectively; NRP1 and NRP2, neuropilin 1 and 2, respectively; NRTN, neurturin; NTF3 and NTF4, neurotrophins 3 and 4, respectively; NTRK1, NTRK2, and NTRK3, neurotrophic receptor tyrosine kinase 1, 2, and 3, respectively; OGFR, opioid growth factor receptor; OPRD1, opioid receptor δ1.

щ	Human		Deficit (↓)	Excess (↑)			
#	Gene	Nsnp	Effect on reproductive potential [Reference]	ď₽	Nsni	Effect on reproductive potential [Reference]	ď₽
215	OPRK1	1 [4]	within a model of human behavior using flocks of male starlings during the breeding season: improved sexual/agonistic aggressiveness [413]	\rightarrow	1 [4]	within a clinical cohort-based study: increased risks of breast cancer [414]	\leftarrow
216	OPRL1	1 [4]	within a model of human behavior using mice: increased risks of fear-related behavior [415]	←	1 [4]	within a clinical cohort-based study: increased risks of pain hypersensitivity [416]	←
217	OPRM1	6 [4]	in human behavior models using Oprm1-knockout mice administered with morphine as OPRM1-agonist: pain hypersensitivity [417]	←	11 [4]	in human men subfertility model using mice sperm incubated with OPRD1- agonist: reduced both fertilization rate and number of reached blastocysts [418	
218	OSM		within a model of women fertility using pregnant mice with artificial injury in endometrium: reduced fertility [419]	←	1 [4]	in human disease models using mice with artificial spinal cord injury treated with exogenous OSM: improved post-injury recovery [417]	$^{\prime} \rightarrow$
219	OSMR	1 [4]	in traditional Chinese medicine, Fei-Yang-Chang-Wei-Yan capsule (FYC) reduces OSMR level to treat gastroenteritis and dysentery [420]	\rightarrow	6 [4]	worsened skin wound healing because of severe pruritus [421]	\leftarrow
220	OXTR	1 [4]	within a model of human behavior using Oxtr-knockout mice: increased intermale aggressive behavior [422]	\rightarrow	2 [4]	in human maternal behavior models using lactating female rats versus nulliparous female mice: increased maternal aggression [423]	\rightarrow
221	PDGFA	1 [4]	in human disease models using mice with artificial atrial fibrillation treated with anti-PDGFA antibody: attenuated atrial fibrosis [424]	\rightarrow		in women fertility models using endometrial biopsies from women undergoing curettage for benign conditions: improved embryo implantation [425]	
222	PDGFB	2 [4]	within a clinical cohort-based ovarian ageing study: increased risks of diminished ovarian reserve [426]	←	6 [4]	within a model of human behavior using transgenic mice overexpressing Pdgfb: increased risks of locomotor dysfunction [427]	_ ←
223	PDGFC	1 [4]	in women subfertility models using mice with artificial intrauterine adhesions injected with human amnion epithelial cells: increased pregnancy rate [428]	\rightarrow		within a clinical cohort-based surgical thyroid tissue biopsie study: increased risks of papillary thyroid carcinomas [429]	←
224	PDGFD	1 [4]	in human disease models using Pdgfd-knockout mice: increased risks of cardiac vasculature disorganization and arterial hypertension [430]	←	2 [4]	within a model of human diseases using transgenic mice overexpressing Pdgfd: improved skin wound healing [431]	\rightarrow
225	PDGFRA	1 [4]	increased risks of skeletal defects in newborns [432]	←	2 [4]	increased risks of fibrotic scar formation in infection and, thereby, infertility [433]	←
226	PDGFRB	1 [4]	within a model of human diseases using Pdgfrb-deficient mice: worsened post traumatic skin wound healing [434]	←	6 [4]	within a model of women fertility using female goats having whether two lambs or one lamb in offspring: improved fertility [435]	$r \rightarrow$
227	PDGFRL		in renal cell carcinoma patients, lesser tumor mutation burden with lesser risks of worse prognosis, tumor metastasis and development [436]	\rightarrow	2 [4]	increased risks of hypertensive behavior and myocardial hypertrophy [437]	^у
228	PDYN		in a model of human infertility using Zucker's fatty female rats, obese reduces Pdyn level compared to Zucker's lean female rats as a norm [438]	←	3 [4]	prevented behavior of conditioned fear [439]	\rightarrow
229	PENK	2 [4]	within a model of human behavior using Penk-knockout mice: increased risks of anxiety-like behavior in acute stress situations [440]	←	11 [4]	within a model of woman puberty using pre- and postpubertal female cattle: accelerated reproductive maturation [441]	$e \rightarrow$
230	PGF	3 [4]	within a model of human development using Pgf-knockout mice treated with PGF-injections: increased risks of depression-like behavior [442]	←	7 [4]	within a model of human fertility using female buffaloes injected with PGF-analog: increased viable embryos rate [443]	$h \rightarrow$
231	PGR	1 [3]	within a model of human diseases using PGR-knockout mice, infertility through embryo attachment impaired [444]	←	1 [3]	improved recidive-free survival after an estrogen receptor positive breast cancer recovery [445]	\rightarrow

<u>*Genes:*</u> OPRK1 and OPRM1, opioid receptor κ1, and μ1, respectively; OPRL1, opioid related nociceptin receptor 1; OSM and OSMR, oncostatin M and its receptor, respectively; OXTR, oxytocin receptor; PDGFA, PDGFB, PDGFC, and PDGFD, platelet-derived growth factor subunits A, B, C, and D, respectively; PDGFRA and PDGFRB, platelet derived growth factor receptor α and β, respectively; PDGFRL, platelet derived growth factor receptor-like protein; PDYN, prodynorphin; PENK, proenkephalin; PGF, placental growth factor.; PGR, progesterone receptor;

	Human		Deficit (↓)		Excess (↑)		
#	Gene	NSNP	Effect on reproductive potential [Reference]	ď₽	Nsn	P Effect on reproductive potential [Reference]	ďŶ
232	PLCXD1	15 [5]	increased risks of ischemic stroke and its complications in men of middle (reproductive) age [446]	\leftarrow	35 [5]	within human cancer models using melanoma cells, transfection of a vector with PLCXD1 gene cDNA inhibits their proliferation [447]	\rightarrow
233	PNOC	1 [4]	within a model of human behavior using adult male mice with artificial pain induction: reduced pain sensitivity [448]	\rightarrow	3 [4]	within a model of men embryogenesis using mice embryos: improve fetal gubernaculum development and testis descent [449]	\rightarrow
234	РОМС	4 [4]	within a model of human behavior using Pomc-deficient mice: increased acute aggressive response to social conflicts [450]	\rightarrow	1 [4]	in human behavior model using mice injected with viral construct carrying POMC: reduced both weight gain & adipose tissue reserves [451]	\rightarrow
235	PPP2R3B	3 [5]	within a model of human diseases using endemic for China carp fish <i>Gobiocypris rarus,</i> impaired spermatogenesis [452]	←	15 [5]	within human cancer models using melanoma cells, transfection of a plasmid with the PPP2R3B gene cDNA inhibits their growth [453]	\rightarrow
236	PROC	2 [3]	increased risks of life-threatening fulminant purpura in newborns [454]	\leftarrow	6 [3]	within a model of human diseases using mice, increased risks of premature pregnancy loss [455]	\leftarrow
237	PSPN		within a model of human diseases using Pspn-deficient mice: hypersensitivity to cerebral ischemia [456]	←	1 [4]	within a model of human behavior using organotypic spinal cord culture: reduced excitotoxic death of motor neurons in overload [457]	\rightarrow
238	P2RY8	2 [5]	increased risks of acute lymphoblastic leukemia in children [458]	←	2 [5]	increased risk of acute leukemia [459]	←
239	RET	3 [4]	in human disease models using Ret-knockout mice embryos: non-viability after birth via impaired development of the respiratory and nervous systems [460]	←	3 [4]	within a model of human diseases using transgenic male mice: increased risks of men sterility through spermatogenesis defects [461]	←
240	RPS4Y2	1 [5]	increased risks of male infertility [462]	←		increased risks of metabolic fatty liver diseases leading to liver cirrhosis and eventually cancer [463]	←
241	SHOX	5 [5]	increased risks of disproportionate short stature and Madelung's deformity as clubhand [464]	←	3 [5]	increased risks of pathoembryogenesis [465]	←
242	SLC6A3	1 [4]	within a model of human behavior using Slc6a3-knockout mice: increased risk-taking behavior [466]	←		in human behavior models using female mice & their male offspring under various diets: higher locomotion level regardless diets [467]	\rightarrow
243	SLC6A4	2 [4]	in models of human health using SLC6A4-knockout mice, improved both neuroplasticity and functioning of the small intestine [468]	\rightarrow	1 [4]	increased risks of depression, anxiety, spatial dullness, and cognitive inertia [469]	←
244	SLC25A6	1 [5]	increased risks of muscular dystrophy [470]	←	4 [5]	increased resistance to human herpesvirus type 5, which increases morbidity and mortality with weakened immunity [471]	\rightarrow
245	SNCA	5 [2]	within a model of human behavior using Snca-knockout mice: functional deficits in the nigrostriatal dopamine system [472]	←	3 [2]	within a model of human behavior using thransgenic mice overexpressing Snca: increased risk of motor deficits [473]	←
246	SOD1	1 [3]	decreased sperm motility and fertility in vivo [474]	←		increased both the bioavailability of copper in the germ cells and their protection against copper toxicity and oxidative stress [475]	\rightarrow
247	SPRY3		enhanced angiogenesis in tumors and cancer [476]	\leftarrow	10 [5]	gender-specifically increased risks of autism among men compared to women [477]	←
248	STAR	1 [3]	increased risks of lipoid congenital adrenal hyperplasia [478]	←		increased risks of primary adrenal tumors [479]	←

<u>Genes</u>: *PLCXD1*, phosphatidylinositol-specific phospholipase C, X domain containing 1; *PNOC*, prepronociceptin; *POMC*, propiomelanocortin; *PPP2R3B*, protein phosphatase 2 regulatory subunit β"β; *PROC*, protein C (synonym: inactivator of coagulation factors Va and VIIIa); *PSPN*, persephin; *P2RY8*, G-protein coupled purinergic P2Y receptor 8; *RET*, Ret protooncogene; *RPS4Y2*, ribosomal protein S4 Y-linked 2; *SHOX*, short stature homeobox; *SLC6A3* and *SLC6A4*, dopamine and serotonin transporters, respectively; *SLC25A6*, adenine nucleotide translocator 3; *SNCA*, synuclein *α*; *SOD1*, superoxide dismutase 1; *SPRY3*, sprouty RTK signaling antagonist 3; *STAR*, steroidogenic acute regulatory protein;.

щ	Human		Deficit (↓)		Excess (↑)		
#	Gene	Nsnp	Effect on reproductive potential [Reference]	ď₽	Nsni	P Effect on reproductive potential [Reference]	ď₽
249	TAC1	1 [4]	within a model of human reproductive health using Tac1-knockout mice: delayed puberty onset [480]	←		within a cohort-based human brain tissue transcriptome study: behavioral dysfunction in depression [481]	\leftarrow
250	TAC3		Tac3 receptor lack mice are subfertilite as a model of human diseases [482]	←	4 [4]	within a model of human fertility using female Damaraland mole-rats, antagonized to the socially induced infertility [483]	\rightarrow
251	TAC4	1 [4]	in human pain behavior models using rats injected with carrageenan: hyperalgesia and increased scratching post-injury behavior [484]	←	2 [4]	within a model of human pain using mice under artificial inflammatory orofacial pain: facial hyperallodynia [485]	^y ←
252	TACR1		within a model of human pain using mice Tacr1-knockout mice: reduced liver fibrosis and biliary inflammation [486]	\rightarrow	1 [4]	within a model of human pain using mice administered with TACR1- agonists: advanced puberty onset [487]	\rightarrow
253	TACR2		within a model of human pain using mice Tacr2-knockout female mice: increased breeding intervals [488]	←	1 [4]	within a clinical cohort-based study: increased risks of recurrent major depressive disorder [489]	\leftarrow
254	TBL1Y		increased risks of violations of both cardiogenesis and heart rate in men [490]	←	2 [5]	decreased risks of violations of both cardiogenesis and heart rate in men [490]	\rightarrow
255	TGFB1	2 [4]	in men subfertility models using busulfan-treated mice, which were next treated with small molecule TGFB1-inhibitor: repaired fertility [491]	\rightarrow		within a clinical cohort-based study: increased rsks of intervertebral disc degeneration [492]	←
256	TGFB2	1 [4]	within a model of human diseases using Tgfb2-knockout mice, increased risks of perinatal mortality [493]	←		impaired neuroregeneration through formation of post-traumatic collagen scar during wound healing [494]	←
257	TGFB3	1 [4]	within clinical study in assisted reproduction technologies, male infertility through reduced semen quality [495]	←	1 [4]	increased risks of infertility <i>via</i> uterine fibroids impairing decidualization [496]	←
258	TGFBI	4 [4]	within a model of human health using Tgfbi-deficient mice: suppressed tumor growth and metastasis [497]	\rightarrow	14 [4]	within a clinical cohort-based histopathological study: increased risks of oral squamous cell carcinoma [497]	←
259	TGFBR1	2 [4]	within a model of human diseases using Tgfbr1-knockout mice: severe aneurysmal degeneration of thoracic aortas [498]	←	4 [4]	in human disease models using primary human gingival fibroblasts ex vivo: improved neuroregeneration in oral tissue wound healing [499]	\rightarrow
260	TGFBR2	2 [4]	according to the ClinVar database, increased risks of thoracic aortic aneurysm and aortic dissection [500]	←		within a clinical cohort-based nasopharyngeal carcinoma tissue study: suppressed nasopharyngeal carcinoma progression [501]	\rightarrow
261	TGFBR3	2 [4]	within a model of human diseases using old male mice under maxillary molar tooth extractions: slowed oral cavity wound healing [502]	←	2 [4]	within a model of human diseases using rats with grafts: accelerated wound healing due to increased vascularization[504]	\rightarrow
262	TH	1 [2]	within a model of women reproductive health using female rats with small litters compared with those with normal litters: subfertility [505]	←		in human disease models using colitis rats treated with electroacupuncture reduced pain hypersensitivity due to suppressed Th expression [506]	÷ ←
263	THBD	1 [3]	increased risks of placental insufficiency and fetal loss [507]	←		exogenous recombinant soluble human thrombomodulin is widely used as a drug against disseminated intravascular blood coagulation [508]	d ←
264	TMSB4Y		increased risks of prostate cancer [509]	←	1 [5]	gender-specific improved tumor suppression in men [510]	\rightarrow
265	TPH2		within a model of human newborn using Tph2-knockout mice: increased risks of mortality in childhood [511]	←	1 [4]	within a model of human behavior using transgenic mice: reduced aggressiveness [512]	~

<u>Genes</u>: *TAC1, TAC3, TAC4, TACR1,* and *TACR2,* tachykinin precursors 1, 3, 4, as well as receptors 1 and 2, respectively; *TBL1Y,* transducin β like 1 Y-linked; *TGFB1, TGFB2,* and *TGFB3,* transforming growth factors β1, β2, and β3, respectively; *TGFBI,* kerato-epithelin (synonym: as transforming growth factor β induced); *TGFBR1, TGFBR2,* and *TGFBR3,* transforming growth factor β receptor 1, 2, and 3, respectively; *TH,* tyrosine hydroxylase; *THBD,* thrombomodulin; *TMSB4Y,* thymosin β4 Y-linked; *TPH2,* tryptophan hydroxylase 2.

#	Human	Deficit (↓)				Excess (↑)				
	Gene	NSNP	Effect on reproductive potential [Reference]	ď₽	NSNP	Effect on reproductive potential [Reference]	ď₽			
266	TPI1	2 [3]	within a model of human diseases using mice, increased risks of asthenospermia [513]	Ļ		increased risks of intrahepatic cholangiocarcinoma as the second most common primary tumor leading to liver cancer [514]	÷			
267	TSPY2	1 [5]	increased risks of male infertility [515]	÷	2 [5]	increased risks of testicular maturation arrest [515]	←			
268	TSPY4		increased risks of spermatogenesis disorders [516]	\leftarrow	1 [5]	a synthetic agonist of gonadotropin-releasing hormone as a drug for male infertility increases TSPY4 level [516]	\rightarrow			
269	USP9Y		within a model of human diseases using mice, reduced sperm quality [517]	←	1 [5]	increased risk of de novo heart failure in men [518]	←			
270	UTY	1 [5]	within a model of human diseases using mice, increased risks of developmental defects in male embryos [519]	←		gender-specifically improve neurogenesis within the treatment of the nervous system in men [520]	\rightarrow			
271	VAMP7	4 [5]	increased overall survival of patients with esophageal adenocarcinoma [521]	←	9 [5]	within a model of human diseases using mice, increased risks of subfertility [522]	←			
272	VEGFA	4 [4]	within a clinical cohort-based study: antioxidant treatment with N- acetylcysteine protect ovarian follicles from ischemia-reperfusion injury due to reduced VEGFA expression [523]	\rightarrow	20 [4]	within a model of human diseases using rats with artificial wounds: improved skin wound healing[524]	\rightarrow			
273	VEGFB		within a model of human embryogenesis using Vegfb-knockout mice: embryonic lethality [525]	←	2 [4]	within a model of human embryogenesis using mice under intracerebroventricular VEGFB administration: improved neurogenesis when brain injury causes central neuronal loss [526]	\rightarrow			
274	ZBED1	1 [5]	increased risks of subfertility through adenovirus excess within spermatozoa in the later stages of infection [527]	←	11 [5]	increased risks of subfertility through adenovirus excess within spermatozoa in the early stages of infection [527]	←			

Table S1	. Cont.
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Genes: TPI1, triosephosphate isomerase 1; TSPY2 and TSPY4, testis specific protein Y-linked 2 and 4, respectively; USP9Y, ubiquitin specific peptidase 9 Y-linked; UTY, ubiquitously transcribed tetratricopeptide repeat containing, histone demethylase UTY Y-linked; VAMP7, vesicle associated membrane protein 7 (synonym: synaptobrevin-like protein 1); VEGFA and VEGFB, vascular endothelial growth factor A and B, respectively; ZBED1, DNA replication-related element binding factor; ZFY, Zinc-finger protein Y-linked.

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[5]

within a model of human diseases using bulls,

reduced spermatozoa motility [528]

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ZFY

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increased risks spermatocyte meiosis arrests leading to their

apoptosis, azoospermia and, ultimately, infertility [529]

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