**ПРИЛОЖЕНИЯ**
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«Анализ особенностей эволюции генов рецепторов клеточной поверхности человека, участвующих в регуляции аппетита, на основе индексов филостратиграфического возраста и микроэволюционной изменчивости»

## Приложение 1

Keywords that were used to search for publications in the PubMed (https://pubmed.ncbi.nlm.nih.gov /) containing data on appetite-regulating genes

| Keywords denoting pathological conditions | Other keywords |
|---|---|
| Hyperphagia | Food intake |
| Bulimia | Feeding behavior |
| Bulimia nervosa | Appetite |
| Hyperorexia nervosa | Hunger |
| Anorexia nervosa | Anorexigenic effect |
| Anorexia | Orexigenic effect |
| Eating disorder | Lean |
| | Satiety |

## Приложение 2

Human genes orthologous to genes encoding cell surface receptors involved in the regulation of food intake in model organisms (the *Receptors_64* set). Genes are listed in alphabetical order

| # | Official symbol of the gene | Gene ID | Official full name | This gene encodes GPCR (1 – yes, 0 – no) |
|---|---|---|---|---|
| 1 | *ADIPOR1* | 51094 | adiponectin receptor 1 | 0 |
| 2 | *AGTR1* | 185 | angiotensin II receptor, type 1a | 0 |
| 3 | *AGTR2* | 186 | angiotensin II receptor type 2 | 1 |
| 4 | *AVPR1A* | 552 | arginine vasopressin receptor 1A | 1 |
| 5 | *BMPR1A* | 657 | bone morphogenetic protein receptor, type 1A | 0 |
| 6 | *BRS3* | 680 | bombesin-like receptor 3 | 1 |
| 7 | *CCKAR* | 886 | cholecystokinin A receptor | 1 |
| 8 | *CCKBR* | 887 | cholecystokinin B receptor | 1 |
| 9 | *CRHR1* | 1394 | corticotropin releasing hormone receptor 1 | 1 |
| 10 | *CRHR2* | 1395 | corticotropin releasing hormone receptor 2 | 1 |
| 11 | *DRD1* | 1812 | dopamine receptor D1 | 1 |
| 12 | *DRD2* | 1813 | dopamine receptor D2 | 1 |
| 13 | *FFAR1* | 2864 | free fatty acid receptor 1 | 0 |
| 14 | *FFAR4* | 338557 | free fatty acid receptor 4 | 0 |
| 15 | *GALR3* | 8484 | galanin receptor 3 | 1 |
| 16 | *GCGR* | 2642 | glucagon receptor | 1 |
| 17 | *GFRAL* | 389400 | GDNF family receptor alpha like | 0 |
| 18 | *GHR* | 2690 | growth hormone receptor | 0 |
| 19 | *GHSR* | 2693 | growth hormone secretagogue receptor | 1 |
| 20 | *GIPR* | 2696 | gastric inhibitory polypeptide receptor | 1 |
| 21 | *GLP1R* | 2740 | glucagon-like peptide 1 receptor | 1 |
| 22 | *GLP2R* | 9340 | glucagon-like peptide 2 receptor | 1 |
| 23 | *GPR119* | 139760 | G-protein coupled receptor 119 | 1 |
| 24 | *GPR17* | 2840 | G protein-coupled receptor 17 | 1 |
| 25 | *GPR171* | 29909 | G protein-coupled receptor 171 | 1 |
| 26 | *GPR26* | 2849 | G protein-coupled receptor 26 | 1 |
| 27 | *GPR61* | 83873 | G protein-coupled receptor 61 | 1 |
| 28 | *GPR88* | 54112 | G-protein coupled receptor 88 | 1 |
| 29 | *GRPR* | 2925 | gastrin-releasing peptide receptor | 1 |
| 30 | *HCRTR1* | 3061 | hypocretin (orexin) receptor 1 | 1 |
| 31 | *HRH1* | 3269 | histamine receptor H1 | 0 |
| 32 | *HRH3* | 11255 | histamine receptor H3 | 0 |
| 33 | *HTR1A* | 3350 | 5-hydroxytryptamine (serotonin) receptor 1A, G protein-coupled | 0 |
| 34 | *HTR2B* | 3357 | 5-hydroxytryptamine (serotonin) receptor 2B, G protein-coupled | 0 |
| 35 | *IL1R1* | 3554 | interleukin 1 receptor, type I | 0 |
| 36 | *INSR* | 3643 | insulin receptor | 0 |
| 37 | *LEPR* | 3953 | leptin receptor | 0 |
| 38 | *LGR4* | 55366 | leucine-rich repeat-containing G protein-coupled receptor 4 | 1 |
| 39 | *MC3R* | 4159 | melanocortin 3 receptor | 1 |
| 40 | *MC4R* | 4160 | melanocortin 4 receptor | 1 |
| 41 | *MCHR1* | 2847 | melanin-concentrating hormone receptor 1 | 1 |

**Окончание Приложения 2**

| # | Official symbol of the gene | Gene ID | Official full name | This gene encodes GPCR (1 – yes, 0 – no) |
|---|---|---|---|---|
| 42 | *NMBR* | 4829 | neuromedin B receptor | 0 |
| 43 | *NMUR2* | 56923 | neuromedin U receptor 2 | 1 |
| 44 | *NPBWR1* | 2831 | neuropeptides B/W receptor 1 | 1 |
| 45 | *NPBWR2* | 2832 | neuropeptides B/W receptor 2 | 1 |
| 46 | *NPY1R* | 4886 | neuropeptide Y receptor Y1 | 1 |
| 47 | *NPY2R* | 4887 | neuropeptide Y receptor Y2 | 1 |
| 48 | *NPY4R* | 5540 | neuropeptide Y receptor Y4 | 1 |
| 49 | *NPY5R* | 4889 | neuropeptide Y receptor Y5 | 1 |
| 50 | *NTRK2* | 4915 | neurotrophic tyrosine kinase, receptor, type 2 | 0 |
| 51 | *NTSR1* | 4923 | neurotensin receptor 1 (high affinity) | 1 |
| 52 | *OPRD1* | 4985 | opioid receptor, delta 1 | 1 |
| 53 | *OPRK1* | 4986 | opioid receptor, kappa 1 | 1 |
| 54 | *OPRL1* | 4987 | opioid related nociceptin receptor 1 | 1 |
| 55 | *OPRM1* | 4988 | opioid receptor, mu 1 | 1 |
| 56 | *OXTR* | 5021 | oxytocin receptor | 1 |
| 57 | *PRLHR* | 2834 | prolactin releasing hormone receptor | 1 |
| 58 | *PTGER4* | 5734 | prostaglandin E receptor 4 | 1 |
| 59 | *QRFPR* | 84109 | pyroglutamylated RFamide peptide receptor | 0 |
| 60 | *RXFP3* | 51289 | relaxin/insulin-like family peptide receptor 3 | 1 |
| 61 | *SCTR* | 6344 | secretin receptor | 1 |
| 62 | *SSTR2* | 6752 | somatostatin receptor 2 | 1 |
| 63 | *TLR2* | 7097 | toll like receptor 2 | 0 |
| 64 | *TLR4* | 7099 | toll like receptor 4 | 0 |

## Приложение 3

The set of genes *Receptors_64* contains an increased number of genes with brain-specific expression pattern. The tissue-specific genes were identified using *TSEA tool* (Wells et al., 2015), expression pattern was considered tissue-specific at pSI < 0.01

| Organ or tissue | Number of genes | Official gene symbols | *p*-value* |
|---|---|---|---|
| Brain | 12 | *NTRK2*, *GPR26*, *GPR88*, *GPR61*, *DRD1*, *HTR1A*, *NPY2R*, *CCKBR*, *OPRK1*, *MC4R*, *DRD2*, *HRH3* | 0.007 |

* Benjamini–Hochberg adjusted *p*-value, derived from a Fisher's exact test was calculated by *TSEA tool*.

## Приложение 4

Genes from the *Receptors_64* set, sorted in ascending order of their PAI values

| # | Official gene symbol | PAI_0.5 | DI | # | Official gene symbol | PAI_0.5 | DI |
|---|---|---|---|---|---|---|---|
| 1 | *NPBWR1* | 0 | 0.047675 | 33 | *GRPR* | 5 | 0.12935 |
| 2 | *NTRK2* | 0 | 0.0994 | 34 | *CRHR1* | 5 | 0.140025 |
| 3 | *OPRD1* | 0 | 0.12515 | 35 | *MCHR1* | 5 | 0.142933 |
| 4 | *HRH3* | 0 | 0.126367 | 36 | *NTSR1* | 5 | 0.17005 |
| 5 | *CCKBR* | 0 | 0.1445 | 37 | *PTGER4* | 5 | 0.178175 |
| 6 | *HCRTR1* | 0 | 0.151725 | 38 | *GPR17* | 5 | 0.22565 |
| 7 | *INSR* | 0 | 0.1539 | 39 | *LGR4* | 5 | 0.242775 |
| 8 | *CCKAR* | 0 | 0.178125 | 40 | *NPY4R* | 5 | 0.245425 |
| 9 | *GPR88* | 0 | 0.19165 | 41 | *OPRL1* | 5 | 0.2486 |
| 10 | *GALR3* | 0 | 0.214275 | 42 | *NPBWR2* | 5 | 0.258825 |
| 11 | *HTR1A* | 0 | 0.30975 | 43 | *MC4R* | 5 | 0.26265 |
| 12 | *GLP2R* | 0 | 0.412825 | 44 | *MC3R* | 5 | 0.2949 |
| 13 | *GIPR* | 0 | 0.551925 | 45 | *RXFP3* | 5 | 0.335725 |
| 14 | *GPR61* | 1 | 0.1193 | 46 | *OPRM1* | 5 | 0.3681 |
| 15 | *GLP1R* | 1 | 0.2556 | 47 | *PRLHR* | 5 | 0.386475 |
| 16 | *SCTR* | 1 | 0.39195 | 48 | *OPRK1* | 5 | 0.449375 |
| 17 | *OXTR* | 1 | 0.463475 | 49 | *NMBR* | 5 | 0.484625 |
| 18 | *ADIPOR1* | 2 | 0.021525 | 50 | *AGTR1* | 5 | 0.486 |
| 19 | *BMPR1A* | 2 | 0.05755 | 51 | *NMUR2* | 5 | 0.56715 |
| 20 | *CRHR2* | 2 | 0.5127 | 52 | *GCGR* | 5 | 0.60365 |
| 21 | *DRD1* | 3 | 0.02565 | 53 | *AGTR2* | 6 | 0.1415 |
| 22 | *GPR26* | 5 | 0 | 54 | *FFAR4* | 6 | 0.2867 |
| 23 | *NPY1R* | 5 | 0.007025 | 55 | *TLR2* | 6 | 0.2968 |
| 24 | *GHSR* | 5 | 0.01945 | 56 | *HRH1* | 6 | 0.317625 |
| 25 | *NPY2R* | 5 | 0.042625 | 57 | *LEPR* | 6 | 0.463275 |
| 26 | *GPR171* | 5 | 0.0446 | 58 | *GPR119* | 6 | 0.4857 |
| 27 | *SSTR2* | 5 | 0.051525 | 59 | *TLR4* | 6 | 0.548 |
| 28 | *DRD2* | 5 | 0.051775 | 60 | *GHR* | 6 | 0.90215 |
| 29 | *BRS3* | 5 | 0.05945 | 61 | *QRFPR* | 6 | 1.210525 |
| 30 | *NPY5R* | 5 | 0.0628 | 62 | *IL1R1* | 7 | 0.2912 |
| 31 | *HTR2B* | 5 | 0.09305 | 63 | *FFAR1* | 7 | 0.37445 |
| 32 | *AVPR1A* | 5 | 0.119 | 64 | *GFRAL* | 7 | 0.512575 |

## Приложение 5

The difference between the observed number of genes from the *Receptors_64* set having PAI = 5 and the expected one, calculated based on data for all human protein-coding genes (the set a*llCDS_19,566*)

| Set or subset of genes | The set of genes | | |
|---|---|---|---|
| | *allCDS_19,566* | *Receptors_64* | |
| | Observed number | Expected number | Observed number |
| All genes from the set | 19556 | 64 | 64 |
| Genes having PAI = 5 | 3330 | 64*3330/19556 = 10.898 | 31 |
| Genes having PAI ≠ 5 | 16226 | 64*16226/19556 = 53.102 | 33 |
| *p*-value (chi-square test) | | | $p < 0.001$ |

## Приложение 6

The difference between the observed number of genes from the *allGPCR_389* set having PAI = 5 and the expected one, calculated based on data for all human protein-coding genes (the set *allCDS_19,566*)

| Set or subset of genes | The set of genes | | |
|---|---|---|---|
| | *allCDS_19,566* | *allGPCR_389* | |
| | Observed number | Expected number | Observed number |
| All genes from the set | 19556 | 389 | 389 |
| Genes having PAI = 5 | 3330 | 389*3330/19556 = 66.239 | 150 |
| Genes having PAI ≠ 5 | 16226 | 389*16226/19556 = 322.761 | 239 |
| *p*-value (chi-square test) | | | $p < 0.001$ |

## Приложение 7

The difference between the observed number of genes from the *appGPCR_45* set having PAI = 5 and the expected one, calculated based on data for all human genes encoding GPCRs (the set *allGPCR_389*)

| Set or subset of genes | The set of genes | | |
|---|---|---|---|
| | *allGPCR_389* | *appGPCR_45* | |
| | Observed number | Expected number | Observed number |
| All genes from the set | 389 | 45 | 45 |
| Genes having PAI = 5 | 150 | 45*150/389 = 17.352 | 28 |
| Genes having PAI ≠ 5 | 239 | 45*239/389 = 27.648 | 17 |
| *p*-value (chi-square test) | | | $p < 0.001$ |

## Приложение 8

The difference between the observed number of genes from the *app_not_GPCR_19* set having PAI = 6 and the expected one, calculated based on data for all human genes encoding GPCRs (the set *allCDS_19,556*)

| Set or subset of genes | The set of genes | | |
|---|---|---|---|
| | *allCDS_19,556* | *app_not_GPCR_19* | |
| | Observed number | Expected number | Observed number |
| All genes from the set | 19556 | 19 | 19 |
| Genes having PAI = 6 | 2769 | 19*2769/19556 = 2.690 | 6 |
| Genes having PAI ≠ 6 | 16787 | 19*16787/19556 = 16.310 | 13 |
| *p*-value (chi-square test) | | | $p < 0.05$ |

## Приложение 9

Genes from the *Receptors_64* set, sorted in ascending order of their DI values

| # | Official gene symbol | PAI_0.5 | DI | # | Official gene symbol | PAI_0.5 | DI |
|---|---|---|---|---|---|---|---|
| 1 | *GPR26* | 5 | 0 | 33 | *LGR4* | 5 | 0.242775 |
| 2 | *NPY1R* | 5 | 0.007025 | 34 | *NPY4R* | 5 | 0.245425 |
| 3 | *GHSR* | 5 | 0.01945 | 35 | *OPRL1* | 5 | 0.2486 |
| 4 | *ADIPOR1* | 2 | 0.021525 | 36 | *GLP1R* | 1 | 0.2556 |
| 5 | *DRD1* | 3 | 0.02565 | 37 | *NPBWR2* | 5 | 0.258825 |
| 6 | *NPY2R* | 5 | 0.042625 | 38 | *MC4R* | 5 | 0.26265 |
| 7 | *GPR171* | 5 | 0.0446 | 39 | *FFAR4* | 6 | 0.2867 |
| 8 | *NPBWR1* | 0 | 0.047675 | 40 | *IL1R1* | 7 | 0.2912 |
| 9 | *SSTR2* | 5 | 0.051525 | 41 | *MC3R* | 5 | 0.2949 |
| 10 | *DRD2* | 5 | 0.051775 | 42 | *TLR2* | 6 | 0.2968 |
| 11 | *BMPR1A* | 2 | 0.05755 | 43 | *HTR1A* | 0 | 0.30975 |
| 12 | *BRS3* | 5 | 0.05945 | 44 | *HRH1* | 6 | 0.317625 |
| 13 | *NPY5R* | 5 | 0.0628 | 45 | *RXFP3* | 5 | 0.335725 |
| 14 | *HTR2B* | 5 | 0.09305 | 46 | *OPRM1* | 5 | 0.3681 |
| 15 | *NTRK2* | 0 | 0.0994 | 47 | *FFAR1* | 7 | 0.37445 |
| 16 | *AVPR1A* | 5 | 0.119 | 48 | *PRLHR* | 5 | 0.386475 |
| 17 | *GPR61* | 1 | 0.1193 | 49 | *SCTR* | 1 | 0.39195 |
| 18 | *OPRD1* | 0 | 0.12515 | 50 | *GLP2R* | 0 | 0.412825 |
| 19 | *HRH3* | 0 | 0.126367 | 51 | *OPRK1* | 5 | 0.449375 |
| 20 | *GRPR* | 5 | 0.12935 | 52 | *LEPR* | 6 | 0.463275 |
| 21 | *CRHR1* | 5 | 0.140025 | 53 | *OXTR* | 1 | 0.463475 |
| 22 | *AGTR2* | 6 | 0.1415 | 54 | *NMBR* | 5 | 0.484625 |
| 23 | *MCHR1* | 5 | 0.142933 | 55 | *GPR119* | 6 | 0.4857 |
| 24 | *CCKBR* | 0 | 0.1445 | 56 | *AGTR1* | 5 | 0.486 |
| 25 | *HCRTR1* | 0 | 0.151725 | 57 | *GFRAL* | 7 | 0.512575 |
| 26 | *INSR* | 0 | 0.1539 | 58 | *CRHR2* | 2 | 0.5127 |
| 27 | *NTSR1* | 5 | 0.17005 | 59 | *TLR4* | 6 | 0.548 |
| 28 | *CCKAR* | 0 | 0.178125 | 60 | *GIPR* | 0 | 0.551925 |
| 29 | *PTGER4* | 5 | 0.178175 | 61 | *NMUR2* | 5 | 0.56715 |
| 30 | *GPR88* | 0 | 0.19165 | 62 | *GCGR* | 5 | 0.60365 |
| 31 | *GALR3* | 0 | 0.214275 | 63 | *GHR* | 6 | 0.90215 |
| 32 | *GPR17* | 5 | 0.22565 | 64 | *QRFPR* | 6 | 1.210525 |

## Приложение 10

The difference between the observed number of genes from the *Receptors_64* set having a low value of DI (DI ≤ 0.6) and the expected one, calculated based on data for all human protein-coding genes (the set *allCDS_19,566*)

| Set or subset of genes | The set of genes | | |
|---|---|---|---|
| | *allCDS_19,566* | *Receptors_64* | |
| | Observed number | Expected number | Observed number |
| All genes from the set | 19556 | 64 | 64 |
| Genes having DI ≤ 0.6 | 15874 | 64*15874/19556 = 51.95 | 61 |
| Genes having DI > 0.6 | 3682 | 64*3682/19556 = 12.05 | 3 |
| *p*-value (chi-square test) | | | $p < 0.01$ |

## Приложение 11

The difference between the observed number of genes from the *appGPCR_45* set having a low DI value (DI ≤ 0.6) and the expected one, calculated based on data for human genes encoding receptors belonging to the GPCRs superfamily (the set *allGPCR_389*)

| Set or subset of genes | The set of genes | | |
|---|---|---|---|
| | *allGPCR_389* | *appGPCR_45* | |
| | Observed number | Expected number | Observed number |
| All genes from the set | 389 | 45 | 45 |
| Genes having DI ≤ 0.6 | 320 | 45*320/389 = 37.018 | 43 |
| Genes having DI > 0.6 | 69 | 45*69/389 = 7.982 | 2 |
| *p*-value (chi-square test) | | | $p < 0.05$ |

## Приложение 12

The difference between the observed and expected numbers of genes in four subgroups of the *Receptors_64* set having (1) different DI values (DI ≤ 0.2 and DI > 0.2) and (2) different expression patterns ("Brain-specific" and "Others").
The expected numbers were calculated based on the number of genes in the *Receptors_64* set, that have brain-specific expression pattern

| Set or subset of genes | Observed number | Expected number | | Observed number | |
|---|---|---|---|---|---|
| | | Brain-specific | Others | Brain-specific | Others |
| All genes from the set or subset | 64 | 12 | 52 | 12 | 52 |
| Genes having DI ≤ 0.2 | 30 | 12*30/64= 5.625 | 52*30/64= 24.375 | 9 | 21 |
| Genes having DI > 0.2 | 34 | 12*34/64 = 6.375 | 52*34/64= 27.625 | 3 | 31 |
| *p*-value (chi-square test) | | | | $p < 0.05$ | |

## Приложение 13

Genes encoding cell surface receptors involved in the regulation of appetite which had the lowest DI (DI < 0.05) and their functional characteristics

| Official gene symbol | PAI | DI | Comment |
|---|---|---|---|
| *GPR26* | 5 | <0.005 | *GPR26* encodes G-protein coupled receptor 26. It is a brain-specific receptor, whose endogenous ligand has not yet been identified (orphan GPCR) with high expression in the brain region that controls satiety. Mice with targeted deletion of the *GPR26* gene demonstrate hyperphagia and decreased energy expenditure (Chen et al., 2012) |
| *NPY1R* | 5 | 0.007025 | The encoded transmembrane protein belongs to the G-protein-coupled receptor superfamily and mediates the function of neuropeptide Y (NPY), a neurotransmitter, and peptide YY (PYY), a gastrointestinal hormone (RefSeq, Aug 2013). Conditional knockout of *Npy1r* gene in the excitatory neurons of the forebrain of adolescent male mice ($Npy1r^{rfb}$ mice) increased body weight, visceral adipose tissue, and blood glucose levels, hyperphagia and a dysregulation of calory intake as compared to control mice (Paterlini et al., 2021) |
| *GHSR* | 5 | 0.01945 | The encoded transmembrane protein belongs to the G-protein-coupled receptor superfamily. Two identified transcript variants are expressed in several tissues and are evolutionary conserved in fish and swine. One transcript, 1a, excises an intron and encodes the functional protein; this protein is the receptor for the Ghrelin ligand and defines a neuroendocrine pathway for growth hormone release. The second transcript (1b) retains the intron and does not function as a receptor for Ghrelin; however, it may function to attenuate activity of isoform 1a (RefSeq, Apr 2010). Ghsr(-/-) mice demonstrated lower food intake, lower body weight, and resistance to high-fat diet-induced obesity (Wang et al., 2018) |
| *ADIPOR1* | 2 | 0.021525 | This gene encodes a protein which acts as a receptor for adiponectin, a hormone secreted by adipocytes which regulates fatty acid catabolism and glucose levels (RefSeq, Mar 2014). In rats the presence of AdipoR1 was mapped to the arcuate and lateral hypothalamic nuclei. Intracerebroventricular injection of adiponectin reduced food intake. This action was dependent on AdipoR1, since inhibition of this receptor, and not of AdipoR2, completely reversed the effects described above (Coope et al., 2008) |
| *DRD1* | 3 | 0.02565 | This gene encodes the D1 subtype of the dopamine receptor which belongs to the G-protein-coupled receptor superfamily. The D1 subtype is the most abundant dopamine receptor in the central nervous system (RefSeq, Jul 2008). The effect of selective D1 dopamine receptor agonists on food consumption were investigated in free-feeding rats. A selective D1 receptor agonist decreased food pellet intake (Martin-Iverson et al., 1988) |
| *NPY2R* | 5 | 0.042625 | This gene encodes the neuropeptide Y receptor type 2 which belongs to the G-protein-coupled receptor superfamily. This receptor mediates the function of neuropeptide Y (NPY), and peptide YY (PYY), a gastrointestinal hormone, neuropeptide Y, a neurotransmitter, and NPY- and PYY-derived peptides (PYY (3-36) > NPY (2-36) etc.) (Mittapalli et al., 2014). Naveilhan P. and coauthors inactivated the Y2 receptor subtype in mice and found that these mice developed increased body weight, food intake and fat deposition (Naveilhan et al., 1999) |
| *GPR171* | 5 | 0.0446 | The protein encoded by *GPR171* belongs to the G-protein-coupled receptor superfamily. GPR171 acts as a receptor for BigLen (b-LEN), a proSAAS-derived peptide (encoded by *PCSK1N*). Peripheral injection of an agonist of GPR171 (MS0015203) into mice increased food intake and body weight, and these responses were significantly attenuated in mice with decreased expression of *GPR171* in the hypothalamus (Wardman et al., 2016) |
| *NPBWR1* | 0 | 0.047675 | The protein encoded by *NPBWR1* belongs to the G-protein-coupled receptor superfamily. Endogenous peptide ligands of these receptors, neuropeptide B (NPB) and neuropeptide W (NPW), have been implicated in regulation of feeding behavior, energy homeostasis, neuroendocrine function, and modulating inflammatory pain (Sakurai, 2013). Intracerebroventricular administration of neuropeptide B stimulated feeding in male rats in a manner similar to that of the other endogenous ligand for NPBWR1, neuropeptide W (Samson et al., 2004) |

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