<table>
<thead>
<tr>
<th><strong>Allele</strong></th>
<th><em>business_class</em></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mutation Type</strong></td>
<td>missense</td>
</tr>
<tr>
<td><strong>Chromosome</strong></td>
<td>4</td>
</tr>
<tr>
<td><strong>Coordinate</strong></td>
<td>101,764,872 bp (GRCm38)</td>
</tr>
<tr>
<td><strong>Base Change (assembly)</strong></td>
<td>T ? A</td>
</tr>
<tr>
<td><strong>Gene</strong></td>
<td><em>Lepr</em></td>
</tr>
<tr>
<td><strong>Gene Name</strong></td>
<td>leptin receptor</td>
</tr>
<tr>
<td><strong>Synonym(s)</strong></td>
<td>obl, Leprb, Obr, obese-like, OB-RGRP, Modb1, leptin receptor gene-related protein, LEPROT</td>
</tr>
<tr>
<td><strong>Chromosomal Location</strong></td>
<td>101,717,404-101,815,352 bp (+)</td>
</tr>
<tr>
<td><strong>Accession Number</strong></td>
<td>NCBI RefSeq: NM_146146, NM_010704; MGI: 104993</td>
</tr>
<tr>
<td><strong>Mapped</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Amino Acid Change</strong></td>
<td>Phenylalanine changed to Isoleucine</td>
</tr>
<tr>
<td><strong>Institutional Source</strong></td>
<td>Beutler Lab</td>
</tr>
<tr>
<td><strong>Phenotypic Category</strong></td>
<td>adipose tissue, behavior/neurological, Body Weight - increased, growth/size, homeostasis/metabolism, reproductive system</td>
</tr>
<tr>
<td><strong>Penetrance</strong></td>
<td>100%</td>
</tr>
<tr>
<td><strong>Alleles Listed at MGI</strong></td>
<td>All alleles (36) : Targeted, knock-out (3) Targeted, other (12) Transgenic (1) Spontaneous (13) Chemically induced (7)</td>
</tr>
</tbody>
</table>

Cite this information as follows: Philippe Georgel, Nora G. Smart, Beutler B. Record for *business_class*, updated Mar 30, 2019. MUTAGENETIX (TM), B. Beutler and colleagues, Center for the Genetics of Host Defense, UT Southwestern Medical Center, Dallas, TX. URL: mutagenetix.utsouthwestern.edu

1 of 22
(Generated on Apr 11, 2019)
### Lab Alleles


### Mode of Inheritance

- Autosomal Semidominant

### Local Stock

- Embryos

### Repository

- MMRRC: 016986-UCD

### Science Writers

- Nora G. Smart

### Authors

- Philippe Georgel, Bruce Beutler

### Illustrators

- Diantha La Vine

### Last Updated

- 03/30/2019 7:46 AM by Diantha La Vine

### Record Created

- unknown

### Record Posted

- 04/22/2008

Cite this information as follows: Philippe Georgel, Nora G. Smart, Beutler B. Record for business_class, updated Mar 30, 2019. MUTAGENETIX (TM), B. Beutler and colleagues, Center for the Genetics of Host Defense, UT Southwestern Medical Center, Dallas, TX. URL: mutagenetix.utsouthwestern.edu

2 of 22

(Generated on Apr 11, 2019)
Phenotypic Description

Figure 1. *Business class* mice are characterized by severe obesity. (A) Photograph of Business class (*db*<sup>333</sup>/*db*<sup>333</sup>) and wild type (WT) littermates. (B) Body weights of *db*<sup>333</sup>/*db*<sup>333</sup> and WT mice at 6 months of age. Figure reproduced from reference (1).

The *Business class* mutation was identified in ENU-mutagenized G3 mice, and is characterized by massive obesity, diabetes, and low fertility in homozygous animals (1) (Figure 1). The mutation is semidominant, with heterozygous animals exhibiting increased mass relative to wildtype animals. This phenotype has not been quantified. The usually sterile homozygotes are propagated from heterozygous stock. Because of the similarity between these animals and the phenotype of mice with leptin or leptin receptor mutations (2-4), direct sequencing was performed and a mutation in the leptin receptor (*Lepr*) gene was found. *Business class* mutants have similar phenotypes to allelic *C herub, Well-upholstered* and *odd* mutants.

Extensive phenotypic characterization of homozygous *business class* mice revealed hyperphagia, significantly elevated circulating levels of leptin, insulin, and the pro-inflammatory cytokine interleukin 6 (IL-6) relative to wild type animals. In addition, they display decreased insulin sensitivity, impaired glucose tolerance, as well as lower core body temperature, locomotor activity, and other metabolic parameters (1).
The *Business class* mutation corresponds to a T to A transversion at position 999 of the *Lepr* transcript (record for variant 1; NM_146146), in exon 7 of 18 total exons.

982 ACACAAGATGTGTTGATTTTCCACCCAAAATT
328 -T--Q--D--V--V--Y--F--P--P--K--I-

The mutated nucleotide is indicated in red lettering and results in the conversion of tyrosine 333 to a stop codon. This removes the C-terminal 829 amino acids of the leptin receptor (LEPR) protein.

**Protein Prediction**

The *Lepr* or *obr* gene encodes an 1162 amino acid protein that is the receptor for leptin, a four-helical cytokine-like hormone produced primarily by adipocytes (2;5). Mouse LEPR, or OB-R (for obesity receptor), is 75% identical to human LEPR (3;6). The leptin receptor is a member of the gp130 family of cytokine receptors that are known to stimulate gene transcription via activation of cytosolic STAT (signal transducer and activator of transcription) proteins. These receptors include the interleukin-6 (IL-6) receptor, the granulocyte colony-stimulating factor (G-CSF) receptor, and the leukemia inhibitory factor (LIF) receptor (3;7).
At least six isoforms of the leptin receptor, designated OB-Ra-OB-Rf, are generated from the Lepr gene through alternative splicing (6;8;9) (Figure 2). With the exception of a soluble isoform (OB-Re), all are single-pass membrane-spanning proteins differing only in the sequences of their C-terminal intracellular domains (6;8-10). Intracellularly, the membrane-spanning leptin receptor isoforms contain a highly conserved proline-rich box 1 (intracellular amino acid 6-17 for the human receptors) (11;12), which may have some signaling function in vitro (13). However, only the longest isoform, OB-Rb, has a 302 amino acid intracellular domain containing all the functional domains.
required to modulate the known intracellular signaling effectors of leptin (see Background) (7;14).

The extracellular portion of the human leptin receptor contains at least seven structural domains that are similar to domains contained in related cytokine receptors (15-17). Domains 1 (amino acids 62-178), and 4 (amino acids 428-535) are CK domains named for their conserved cysteine-containing motifs. Domains 2 (amino acids 235-327), 5 (amino acids 536-635), 6 (amino acids 636-731), and 7 (amino acids 732-841) each possess a fibronectin type III fold. Domain 3 (amino acids 328-427) has an Ig-like fold. Domains 1 and 2 form the cytokine receptor homology module 1, while domains 4 and 5 form the cytokine receptor homology module 2. These modules each contain a cytokine-like binding motif, Trp-Ser-Xaa-Trp-Ser (3;15). The fibronectin type III domains are predicted to be composed of ?-strands that form anti-parallel ?-sandwiches (17). Despite the structural prediction that LEPR might have two ligand-binding sites, its sole leptin binding domain is in the second cytokine receptor homology module spanning residues 428-635. The purified leptin-binding subdomain forms a stable 1:1 complex with leptin, although other reports suggest the leptin/leptin receptor complex exists in a 2:4 stoichiometry with two leptin receptor proteins required to bind one leptin molecule (16;18;19). Using the GCSF/GCSFR 2:2 crystal structure as a model, the binding of leptin to the receptor reveals two interaction interfaces. The major interface consists largely of hydrophobic and polar interactions. The minor interface also has a number of hydrophobic interactions, but uses main-chain hydrogen bonding as well (19;20). Alternatively, a structural model of a 2:4 leptin/leptin receptor complex based on the crystal structure of IL-6/IL-6Ra/gp130 complex reveals three binding sites (I, II, III) on leptin. Binding site I appears at the C-terminal region of helix D of the leptin molecule, binding site II is composed of residues at the surface of helices A and C, and binding site III is close to the N-terminal region of helix D (16).

The Business class mutation results in protein truncation at amino acid 333. This deletes most of the protein including the long C-terminal domain important for intracellular signaling, the membrane spanning region, and much of the extracellular region including the ligand-binding region.

Cite this information as follows: Philippe Georgel, Nora G. Smart, Beutler B. Record for business_class, updated Mar 30, 2019. MUTAGENETIX (TM), B. Beutler and colleagues, Center for the Genetics of Host Defense, UT Southwestern Medical Center, Dallas, TX. URL: mutagenetix.utsouthwestern.edu
The short receptor isoforms of the leptin receptors are generally the most abundant forms in most tissues, except the hypothalamus (3;21). In the hypothalamus, the most abundant leptin receptor is OB-Rb, which is expressed in areas important for regulation of energy balance such as arcuate (ARC), paraventricular (PVN), dorsomedial (DMN), and ventromedial (VMH) nuclei (22-25). Expression of Ob-Rb also occurs in other brain regions such as the hippocampus, cerebral cortex, and the choroid plexus from which the leptin receptor was cloned (3;23-26). The OB-Rb receptor is also found in lungs, kidneys, liver, pancreatic β-cells, thyroid gland, anterior pituitary, placenta, adrenal glands, gonads, and vasculature (21;27-35). Finally, OB-Rb is expressed on the surface of immune system cells involved in innate and adaptive immunity including dendritic cells (DC), T lymphocytes, NK cells, as well as hematopoietic stem cells and B cell progenitors (35-37).

During development, expression of leptin receptor isoforms is highly dynamic and varies from species to species. In rat brains at embryonic day (E) 14, cells immunoreactive for OB-Rb are observed in the ventricular layer containing immature neuronal cells. At 18 days of gestation, low levels of staining occurred in the paraventricular nucleus (PVN), and ependymal cells. At birth, the immunoreactivity of OB-Rb in the PVN appears to be much lower than that in adult rats, and remained low during the suckling period (38). In addition, rat neonatal pituitary gland expresses leptin receptors at levels far in excess of those observed in mature rats (39). In the mouse, Ob-Rb mRNA was detected in the brain by RT-PCR at E10.5. Using in situ hybridization, Ob-Rb mRNA was observed in the ventricular zone of the rhombencephalon at E11.5. At E12.5, it was also expressed in the ventricular zone of the telencephalon, mesencephalon, and cerebellar primordium. From E14.5, it was expressed in the cortical plate of the telencephalon, and the ventricular zone of the thalamus. At E16.5, Ob-Rb was expressed in the premamillary hypothalamic nucleus, superficial gray matter of the superior colliculus, external germinal and Purkinje cell layers of the cerebellum, and facial nucleus. At E18.5, it was expressed in the arcuate nucleus and ventromedial hypothalamic nucleus, similar to the adult (40). In peripheral embryonic mouse tissues, an in situ hybridization probe recognizing all Lepr isoforms was found in developing bone, mesenchyme, notochord, liver, as well as epithelial structures (27;41). Lepr mRNA was detected at higher levels in peripheral tissues of newborn mice than in adult mice (42).

**Background**

Leptin, a systemic hormone, regulates multiple functions of the body including energy utilization and storage, various endocrine axes, bone metabolism, thermoregulation, angiogenesis, immunity and
inflammation [reviewed in (19;34;36)]. It is primarily produced by adipocytes in proportion to fat stores, but can also be produced by placenta (syncytiotrophoblasts), ovaries, skeletal muscle, stomach, mammary epithelial cells, bone marrow, pituitary and liver (43). Leptin exerts its action on the body by binding to the long form of the leptin receptor, OB-Rb, and initiating various signal transduction pathways (6-9;13). Several putative functions for the short leptin receptor isoforms have been hypothesized. Some evidence suggests that OB-Ra is responsible for the transport of leptin across the blood-brain barrier (11), whereas the soluble OB-Re binds and stabilizes circulating leptin (44;45). The major functions of all short isoforms, except OB-Re, appear to be limited to leptin transport, internalization and degradation (46). In vitro evidence suggests that they are capable of triggering certain signaling events, as they all contain a highly conserved proline-rich box region that recruits and binds Janus kinases (JAKs) (11-13). Since only the long receptor isoform, OB-Rb, contains the full intracellular signaling sequence, it is the only receptor isoform mediating leptin signaling in vivo (6-9;13;47).
Figure 3. Signaling activated by leptin. See text for details.
Figure 4. Agrp/Npy neurons and Pomc/Cart neurons are located in the arcuate nucleus of the hypothalamus and are regulated by leptin from adipose tissue. Both Agrp/Npy and Pomc/Cart neurons synapse onto MC4R-expressing neurons in the hypothalamus. Agouti and Agrp are hypothalamus-specific antagonists of MC3R and MC4R while ?-MSH, a proteolytic product of Pomc, is a known agonist of MC3R and MC4R. Agrp and Npy stimulate food intake and decrease energy expenditures, causing weight gain. Pomc and Cart inhibit food intake and increase energy expenditure. Agrp, Agouti-related protein; Agrp, producing Agrp; Npy, neuropeptide Y; Pomc, pro-opiomelanocortin; Cart, cocaine- and amphetamine-regulated transcript; ?-MSH, ?-melanocyte stimulating hormone; LEPR, leptin receptor.

Upon leptin binding to OB-Rb, activation of JAK2 at the OB-R box 1 motif is activated (11;14) (Figure 3). JAK2 auto-phosphorylates itself, as well as specific tyrosine residues on the intracellular domain of OB-Rb (Tyr974, Tyr985, Tyr1077 and Tyr1138) to provide docking sites for signaling.
proteins containing Src homology 2 (SH2) domains. Each phosphorylated tyrosine residue then recruits and activates a distinct set of downstream signaling proteins. The phosphorylated tyrosine residues Tyr1077 and Tyr1138 bind and activate signal transducer and activator of transcription (STAT) proteins. Both Tyr1077 and Tyr1138 bind to STAT5, while only Tyr1138 recruits STAT1 and STAT3 (36,48). The other two phosphorylated residues Tyr974 and Tyr985 recruit SH2 domain-containing phosphatase 2 (SHP2). SHP2 then activates the mitogen-activated protein kinase (MAPK) pathways including extracellular signal-regulated kinase (ERK1/2), p38, MAPK and p42/44 MAPK pathways through interaction with the adaptor protein growth factor receptor-bound protein 2 (GRB2) (48-50). The auto-phosphorylated JAK2 at the box 1 motif can phosphorylate insulin receptor substrate1/2 (IRS1/2) that leads to activation of phosphatidylinositol 3-kinase (PI3K)/Akt and the MAPK pathways. OB-Rb has also been reported to signal via the AMP-activated protein kinase (AMPK) pathway (10;49-51). OB-Rb activation induces transcription of the specific suppressor of SOCS3 in the hypothalamic area by direct binding of STAT3 to its response element (49;52). SOCS3 is an SH2 domain-containing protein that can bind phosphorylated Tyr985 on OB-Rb and other sites on JAK2 to inhibit leptin receptor signaling. This negative feedback loop via SOCS3 is speculated to be central to the development of leptin resistance that occurs in many obese subjects due to the high circulating levels of leptin caused by increased fat stores (52;53).

In the hypothalamus, leptin binding to OB-Rb on the appropriate neurons, including the ARC and VMH nuclei, causes diminished feeding activity, and accelerated basal metabolic rate by regulating numerous neuropeptides involved in feeding. Two sets of neurons act as sensors of whole-body energy status, and initiate signals to maintain energy stores at a constant level (Figure 4). The AgRP/NPY neurons (producing agouti-related peptide and neuropeptide Y) are inhibited by leptin, while POMC/CART neurons (producing pro-opiomelanocortin, its proteolytic products, and cocaine-amphetamine-regulated transcript) are stimulated by leptin. Both AgRP/NPY and POMC/CART neurons synapse onto neurons expressing melanocortin receptors 3 and 4 (MC3R, MC4R). POMC is the precursor of various peptides that activate MC3R and MC4R. When leptin levels are low, AgRP/NPY neurons are activated and POMC/CART neurons are inhibited, producing AgRP but not POMC. Consequently, melanocortin receptors are inhibited and food intake increases (54-57). The melanocortin receptors are critical in maintaining body weight regulation. Mutations in both MCR3 and MCR4 (mutated in Southbeach) cause obesity in humans and animals, and MCR4 mutations are a common cause of obesity in humans (58-60).

Other CNS functions of leptin include direct leptin signaling in areas of the brain regulating motivation to feed, and indirect regulation of gonadotropin-releasing hormone (GnRH) neurons of the neuroendocrine reproductive axis, and of the activity of the sympathetic nervous system. Leptin...
also regulates the hypothalamic-pituitary-adrenal (HPA) axis by affecting hypothalamic corticotropin-releasing hormone (CRH) neurons, which subsequently modulate the release of glucocorticoids from the adrenal cortex (34;55). Leptin also regulates the expression of genes important for thermogenesis, such as thyrotropin-releasing hormone (TRH). A subgroup of TRH neurons in the paraventricular nucleus is activated directly by leptin through STAT3 binding to a response element in the TRH promoter (61;62). TRH is essential for pituitary gland production of thyroid-stimulating hormone, as well as thyroid gland synthesis of thyroid hormone. Thyroid hormone is well recognized as a stimulator of energy expenditure through increasing basal metabolic rate (33). Finally, leptin signaling in the brain appears to have important anti-apoptotic effects (63). Indeed, many of the signaling pathways activated by leptin through the leptin receptor are anti-apoptotic and growth-promoting, and leptin signaling has been shown to promote survival and growth in many cell types including cells of the immune system (35;63).

Leptin also plays a role in inflammatory and immune responses. Behaving as a cytokine and activating JAK/STAT signaling in immune cells, leptin has been shown to provide a proliferative signal in hematopoiesis and lymphopoiesis, and appears to have an effect on the differentiation and survival of many types of immune cells including thymocytes (T cells), natural killer (NK) cells, and dendritic cells (DC) (30;35;36;64). Leptin activates monocytes, DC and macrophages, and stimulates them to produce Th1-type cytokines (30;64). Leptin can also activate neutrophils, and NK cells. By activating STAT3, leptin upregulates the expression of genes encoding perforin and IL-2, which are necessary for NK function (37). Importantly, leptin has been shown to modulate adaptive immunity by enhancing T-cell survival and stimulating their production of pro-inflammatory cytokines such as IFN-? and IL-2 (35). Recent evidence demonstrates a detrimental involvement of leptin in promoting the pathogenesis of various autoimmune diseases such as rheumatoid arthritis, colitis, multiple sclerosis and Type 1 diabetes, consistent with its role as a pro-inflammatory cytokine (36). Despite evidence suggesting that leptin and its receptor can have a direct role in immune system modulation (36), other work suggests that the primary effects of leptin on immunity and inflammation are secondary to its effects on the CNS. Through the use of bone marrow chimaeras and thymus transplantation experiments, expression of the leptin receptor on either bone marrow-derived cells or thymic epithelial cells was shown to be unnecessary for normal T-cell development (65). Moreover, in contrast to its direct pro-inflammatory role in the immune system, leptin has an anti-inflammatory effect during systemic inflammation through activation of the HPA axis and modulating glucocorticoids (53).

Humans and other animals deficient for leptin or its receptor, exhibit hyperphagia and low metabolism that results in obesity and insulin resistance (2;6;66). They also display characteristics
similar to the starvation response despite their obesity, including hypothyroidism, infertility, decreased growth, cold intolerance, and decreased immune function (2;3;66). Several rat and mouse leptin receptor mutants exist, including the classic db/db mouse mutant, which is defective for the long form of LEPR (8;9;67). Db/db mutants have highly similar phenotypes from mutants null for the leptin receptor (db^3j/db^3j), suggesting that the short forms of the leptin receptor play only minor roles in vivo (47;67). In addition to the classical leptin receptor mutants, several transgenic, tissue-specific knockout, and knock-in leptin receptor mice have been generated to examine the role of leptin and leptin signaling in vivo. By using tissue-specific knockout mice and transgenic overexpression of ObRb in the brain to rescue leptin receptor mutant mice, the role of leptin signaling in the CNS versus peripheral tissues has been examined (47;67-71). Although it is clear that leptin signaling in peripheral tissues can have an effect on whole-body metabolism, leptin signaling in CNS neurons plays a far more important role in energy balance and homeostasis. Transgenic expression of the leptin receptor in the brain is sufficient to reverse the obesity, diabetes, and infertility of db/db mice (69). Finally, mice that express only OB-Rb mutated at specific tyrosine residues exhibit different phenotypes, suggesting specific roles of the various leptin receptor signal transduction pathways. Knock-in mice expressing a leptin receptor mutated at Tyr1138, which signals through STAT3, are hyperphagic and obese, but have normal fertility and immune function (72;73). Mice expressing a leptin receptor mutant for Tyr985 are lean, consistent with the binding of the negative regulator SOCS3 to this site to downregulate leptin signaling (74).

The phenotypes of a number of knockout animal models have also given insights into the roles of various leptin receptor signal transduction pathways. STAT1-deficient mice (see domino and poison) are not obese, but they do have increased bone mass as do LEPR mutants, although these phenotypes may occur through different mechanisms (75;76). STAT3 knockout animals are embryonic lethal, but neuronal-specific knockouts are hyperphagic, obese, diabetic, and infertile (77). Similarly, neuronal-specific knockouts of SH2-B, a JAK-interacting protein, and SHP2 are also obese (78;79). STAT5 knockout mice reveal roles for STAT5 in mammary development, fertility, and sexually dimorphic growth hormone effects, which may be partially due to a role in leptin receptor signaling (80).

Mutations affecting the leptin receptor are not a major cause of human obesity, and only a small number of patients show destructive mutations at the LEPR locus (66) (OMIM #601665 *601007). LEPR polymorphisms have been found to be associated with human obesity and impaired glucose homeostasis, but make a minor contribution to these phenotypes as a whole, consistent with etiologic complexity of both phenotypes in humans (81;82).

Cite this information as follows: Philippe Georgel, Nora G. Smart, Beutler B. Record for business_class, updated Mar 30, 2019. MUTAGENETIX (TM), B. Beutler and colleagues, Center for the Genetics of Host Defense, UT Southwestern Medical Center, Dallas, TX. URL: mutagenetix.utsouthwestern.edu

13 of 22
(Generated on Apr 11, 2019)
Putative Mechanism

The *Business class* mutation results in early truncation of the leptin receptor. As the mutant protein is missing most of the leptin receptor functional domains including the ligand-binding region, it is not expected to have any function, and should behave like the *db*\(^{3j}\) mice, which are null for all known leptin receptor isoforms (67). Indeed the phenotypes seen in *Business class* homozygotes are highly similar to the phenotypes seen in both homozygous *db* and *db*\(^{3j}\) mutant mice (6;67). However, *business class* homozygous animals display a subtle trend toward higher body weight and insulin levels, lower oxygen, carbon dioxide production, respiratory exchange ratio (RER), and temperature than *db/db* mice suggesting that the short isoforms of the leptin receptor may play additional roles in energy homeostasis (1). *Business class* mutants also have phenotypes similar to *Cherub* and *Well-upholstered* animals. Both of these mutations result in truncation of LEPR in the CRH2 domain (Figure 2).
Business class genotyping is performed by amplifying the region containing the mutation using PCR, followed by sequencing of the amplified region to detect the single nucleotide transition. The same primers are used for PCR amplification and for sequencing.

**Primers**

Bus(F): 5’- GCTGGAAGCCTGTCGTACTCTTCAC -3’
Bus(R): 5’- TACACTGCGTCATAGGTAAACTTCCCTC -3’

**PCR program**

1) 94°C 1:00
2) 94°C 0:30
3) 58°C 0:30
4) 72°C 1:00
5) repeat steps (2-4) 35X
6) 72°C 5:00
7) 4°C ?

The following sequence of 456 nucleotides (from Genbank genomic region **NC_000070** for linear genomic sequence of *Lepr*) is amplified:

```
47204  gctggaa gctggtcga
47221  cttcaggg aggtgtgtc tattgggag caggggtc
47281  cagaagctc tattgcagc attgatttt ggaggggtaa caggcagct
47341  gcataetttt etttggtga aagctgtcga gatgagtggt tgtttctct ttaaactcc
47401  caccttcctt tctctgatc atggttgttg tattttccac cccaaattct gactagttgt
47461  ggttcagagt ctttttct ttgcatctac aaattccta ccaggttcat cctgcttct cctgcttct cctgcttct cctgcttct
47521  cagatagttt gttcagggga ttgatccttg agatacgtt cagcattgtg
47581  agtgacccag ttagcaagt tacctcttcc aacactgaag ccaccagacc tcagggaaag
47641  tttacctatg acgcagtcga
```

Primer binding sites are underlined; the mutated T is highlighted in red.

**References**

Cite this information as follows: Philippe Georgel, Nora G. Smart, Beutler B. Record for business_class, updated Mar 30, 2019. MUTAGENETIX (TM), B. Beutler and colleagues, Center for the Genetics of Host Defense, UT Southwestern Medical Center, Dallas, TX. URL: mutagenetix.utsouthwestern.edu

15 of 22
(Generated on Apr 11, 2019)


