

Selank

A tuftsin-related neuroactive heptapeptide

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Medical review

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ABSTRACT

The sequence produces measurable transcriptional and circuit-level responses connected to GABA-related and neuroimmune systems.

This monograph evaluates Selank, the synthetic tuftsin-related heptapeptide Thr-Lys-Pro-Arg-Pro-Gly-Pro. It distinguishes intranasal human observations from parenteral animal experiments and from the biology of tuftsin itself.

This monograph begins with the molecule and follows the causal chain through biochemistry, cellular mechanism, exposure and integrated physiology. Population studies enter only at the terminal stress-test: useful for the proposition actually tested, incapable of defining the molecule or replacing the causal model.

ESTABLISHED	UNRESOLVED
• Defined heptapeptide • Preclinical GABA-related programme • Intranasal human administration reported	• Human route-specific PK • Controlled clinical magnitude • Parenteral exposure and safety

EVIDENCE HIERARCHY

Mechanistic evidence is not a lower-grade substitute for population medicine. Physical constraints, biochemical measurements, historical and non-English records, exposure studies and clinical outcomes answer different questions. Controlled clinical trials test the complete implemented proposition; they cannot manufacture a missing identity, mechanism or exposure bridge.

I	Molecular identity and chemistry
II	Biochemistry and target architecture
III	Cells and ex-vivo tissues
IV	Animal and in-vivo pharmacology
V	Integrated physiology and translation
VI	Human PK and observational signal
VII	Controlled clinical trials

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ACTION LEDGER

Describe the action before judging its value.

Benefit is a downstream clinical judgement. The scientific object is the action itself: what moves, under which exposure, in which biological state, and where the inference stops.

01 Attributed biochemical action	The sequence produces measurable transcriptional and circuit-level responses connected to GABA-related and neuroimmune systems.
02 Exposure and reachability	Route-specific systemic exposure and human pharmacokinetics are limited. Evidence from intranasal administration cannot establish injectable pharmacology.
03 Physiological direction is contextual	Anxiety, attention and cognitive control arise from distributed neural and immune networks rather than one transmitter concentration. GABA-related transcription, neurotrophic signalling, autonomic state, sleep and inflammatory context may converge, but an acute network change is not equivalent to durable functional regulation. Route-specific exposure remains the bridge between molecular signal and brain physiology.
04 Individual adjudication boundary	A proximal binding model and replicated human route-specific exposure-response relationship. Gene-expression similarity to GABA or an imaging change does not prove benzodiazepine-like pharmacology, durable anxiolysis or injectable efficacy.

METHODS AND COVERAGE

A reproducible boundary, not an implied exhaustive review.

This curated mechanistic monograph uses primary indexed records and reference-chaining. It does not claim systematic-review completeness. Absence of a retrieved result is not evidence that an effect is absent.

SEARCH SURFACE	PubMed/MEDLINE primary records, Russian-language indexed abstracts, and reference-chaining for entity-defining, historical and translational studies. Language, geography, regulatory status and journal fashion are not evidence grades.
QUERY FRAME	Selank · tuftsin analogue · anxiety · GABA · BDNF · intranasal peptide · functional connectivity
EVIDENCE CUTOFF	24 August 2026
ENTITY EXCLUSION	Selank, tuftsin and Selank fragments are related but distinct. Intranasal human administration and parenteral animal administration cannot share exposure assumptions.
TRACEABILITY	12 extended claim units plus 2 historical records and 3 mechanistic-calculus records; 8 cited records in the complete corpus.
INTERPRETIVE RULE	Identity → physical constraint → measured reaction or binding → reachable exposure → system response → outcome. Statistical significance does not manufacture mechanism; mechanistic plausibility does not manufacture a patient outcome.

EVIDENCE ATLAS

Every claim keeps its experimental address.

12 claim units are mapped to evidentiary layer, experimental frame and source records. The layer describes the question answered; it is not a popularity score.

LAYER	EXPERIMENTAL FRAME	FINDING AND BOUNDARY	SOURCES
VIHuman exposure or signal	Sequence and relationship to tuftsin · claim 1	Selank contains the tuftsin sequence Thr-Lys-Pro-Arg extended by Pro-Gly-Pro. The extension can change stability, tissue exposure and biological action. Tuftsin literature may support a mechanistic family relationship but cannot be treated as direct evidence for Selank.	[1][3]
VIHuman exposure or signal	Sequence and relationship to tuftsin · claim 2	Human reports principally concern intranasal administration, while many mechanistic experiments use intraperitoneal dosing in rodents. Those routes create different absorption, concentration-time and tissue-distribution questions. Route is therefore part of the evidence identity.	[1][2][4]
IVIntegrated in-vivo model	GABA-related transcriptional programme · claim 1	In rat frontal cortex, Selank and GABA produced correlated changes in expression of genes involved in neurotransmission. Forty-five genes changed one hour after administration and twenty-two at three hours in the reported experiment. This supports interaction with GABA-related regulatory networks without demonstrating direct benzodiazepine-site agonism.	[2]
VIHuman exposure or signal	GABA-related transcriptional programme · claim 2	Gene-expression similarity is a mechanistic clue, not proof of identical pharmacology or clinical effect. Receptor binding, circuit function, behavioural output and human anxiety symptoms remain separate levels of inference.	[2]
IVIntegrated in-vivo model	Neurotrophic and immune-linked mechanisms · claim 1	Rodent experiments have connected Selank with BDNF regulation, memory behaviour and monoaminergic balance under stress or injury models. These findings broaden the hypothesis beyond acute anxiolysis but remain preclinical and model dependent.	[5]
IVIntegrated in-vivo model	Neurotrophic and immune-linked mechanisms · claim 2	Mouse spleen studies found changes in inflammation-related gene expression after Selank or its fragments, including time-dependent changes in C3, Casp1, Il2rg and Xcr1. This supports immune-neural pleiotropy but does not identify a validated clinical immune indication.	[4][6]

LAYER	EXPERIMENTAL FRAME	FINDING AND BOUNDARY	SOURCES
VIHuman exposure or signal	Human anxiety signal · claim 1	A comparative study enrolled 60 patients with phobic-anxiety, generalised-anxiety and somatoform diagnoses and reported anxiolytic and mild nootropic effects relative to phenazepam, with persistence after treatment. The indexed abstract does not fully resolve randomisation, allocation concealment, blinding or endpoint hierarchy.	[1]
VIHuman exposure or signal	Human anxiety signal · claim 2	The report establishes a human clinical signal worth reproducing. It does not establish effect magnitude against modern comparators or placebo, does not define long-term recurrence and cannot support an injectable claim.	[1]
VIHuman exposure or signal	Human neurophysiology · claim 1	A resting-state functional-connectivity study of 52 healthy participants examined Selank, Semax and placebo and reported changes involving the right amygdala and temporal regions. Imaging demonstrates a measurable neural response but is not a clinical anxiety endpoint.	[7]
VIHuman exposure or signal	Human neurophysiology · claim 2	Small imaging experiments are sensitive to preprocessing, multiplicity and timing. They can refine circuit hypotheses and dose windows; they cannot establish durable symptom benefit, comparative efficacy or safety in a patient population.	[7]
VIIControlled human proposition	Translation boundary · claim 1	Selank has exact molecular identity, a coherent preclinical programme and limited human intranasal signals. Missing elements include route-specific PK, robust placebo-controlled outcomes, repeated-use safety and independent replication outside a concentrated research network.	[1][2][7]
VIHuman exposure or signal	Translation boundary · claim 2	The correct conclusion is not that mechanism is absent. It is that the chain from sequence to human exposure to reproducible patient benefit remains incomplete. Each additional route constitutes a new pharmacological experiment.	[1][2]

SECTION 01

Molecular dossier: the entity before the outcome

ENTITY — Thr-Lys-Pro-Arg-Pro-Gly-Pro, a tuftsin-related heptapeptide

BIOCHEMICAL CLASS — Neuroimmune regulatory peptide

PRIMARY SYSTEM — GABA-related transcription · neurotrophic signalling · immune-neural communication

IDENTITY BOUNDARY — Selank, tuftsin and Selank fragments are related but distinct. Intranasal human administration and parenteral animal administration cannot share exposure assumptions.

SECTION 02

Historical and international corpus

Selank emerged from the Soviet/Russian regulatory-peptide tradition and has decades of Russian preclinical and clinical work. The exact molecule is not 100 years old, but a PubMed-only English-language scan materially understates its research history.

Russian-language indexed records are scientific evidence, not an administrative footnote. Their methods, comparators, route and reporting completeness must be appraised individually rather than accepted or discarded by geography.

SECTION 03

Soviet/Russian peptide lineage: Tuftsin biology was converted into a stabilised regulatory peptide

Selank extends the tuftsin tetrapeptide with Pro-Gly-Pro. This programme arose from a research tradition focused on short regulatory peptides, stress physiology and intranasal delivery; family history informs design but does not replace Selank-specific experiments.[2][3]

SECTION 04

2008 onward: Russian clinical and comparative records must remain visible

A Russian-language comparative report in 60 patients and other clinical reports provide direct human information on intranasal use, psychometric outcomes and biological correlates. Limited blinding and reporting detail reduce precision; they do not turn the studies into no evidence.[1][8]

SECTION 05

Mechanistic calculus — CONSTRAINED: Sequence extension changes the entity

Adding Pro-Gly-Pro to tuftsin changes molecular mass, cleavage sites and potential exposure. A tuftsin effect can motivate a Selank hypothesis but cannot close it.[3]

SECTION 06

Mechanistic calculus — MEASURED: Network response is broader than one receptor

GABA-related transcription, BDNF-linked effects, monoaminergic observations and immune gene responses indicate a distributed regulatory programme. Similarity to GABA does not demonstrate binding at a benzodiazepine site.[2][4][5][6]

SECTION 07

Mechanistic calculus — MEASURED: Clinical signal and mechanism were measured together

The Russian comparative study paired symptom scales with serum leu-enkephalin activity. This is mechanistically richer than a symptom-only report, while still insufficient to establish blinded placebo effect size or durable recurrence prevention.[8]

SECTION 08

Causal architecture: Sequence extension creates a new entity

Selank contains the tuftsin tetrapeptide followed by Pro-Gly-Pro. The extension can alter proteolytic stability, tissue distribution and activity. Tuftsin findings provide family context but cannot be cited as direct Selank evidence.[1][3]

SECTION 09

Causal architecture: GABA-related does not mean GABA-equivalent

Rodent cortical transcription after Selank overlaps with parts of the GABA response. This supports network interaction, while leaving direct receptor binding, circuit localisation and human symptom translation as separate questions.[2]

SECTION 10

Causal architecture: Neuroimmune pleiotropy is plausible

BDNF-related, monoaminergic and spleen gene-expression findings suggest that the peptide can influence more than one biological compartment. Pleiotropy increases explanatory possibilities but also makes a single universal mechanism less defensible.[4][5]

SECTION 11

Causal architecture: Route is a causal variable

Human observations principally use intranasal delivery, whereas much mechanistic work uses other routes in animals. Mucosal absorption, degradation and brain/systemic exposure must be measured before route-to-route conclusions are permitted.[1][2]

SECTION 12

Molecular identity and entity resolution

Selank is a synthetic heptapeptide related to tuftsin. The clinically reported intranasal route and any proposed parenteral route are different exposure experiments.

SECTION 13

Biochemical mechanism and target architecture

Proposed actions include GABAergic modulation, neurotrophic pathways and immune-neural communication. Much of the causal programme remains preclinical.

SECTION 14

In-vivo pharmacology and exposure

Route-specific systemic exposure and human pharmacokinetics are limited. Evidence from intranasal administration cannot establish injectable pharmacology.

SECTION 15

Integrated physiology and individual terrain

Anxiety, attention and cognitive control arise from distributed neural and immune networks rather than one transmitter concentration. GABA-related transcription, neurotrophic signalling, autonomic state, sleep and inflammatory context may converge, but an acute network change is not equivalent to durable functional regulation. Route-specific exposure remains the bridge between molecular signal and brain physiology.

SECTION 16

Terminal human stress-test

A comparative report in 60 patients with anxiety and somatoform disorders described anxiolytic and mild cognitive effects relative to phenazepam, but accessible reporting leaves randomisation, blinding, allocation and endpoint hierarchy insufficiently resolved.

SECTION 17

Counterevidence and causal boundaries

Small human reports establish administration and a signal worth studying; they do not establish broad anxiolysis, cognitive enhancement or injectable efficacy.

SECTION 18

Scientific conclusion

Selank has a partial mechanistic chain and limited, route-bound human evidence. Scientific translation requires route-specific PK, tolerability, systemic exposure and controlled outcomes.

SECTION 19

Sequence and relationship to tuftsin

Selank contains the tuftsin sequence Thr-Lys-Pro-Arg extended by Pro-Gly-Pro. The extension can change stability, tissue exposure and biological action. Tuftsin literature may support a mechanistic family relationship but cannot be treated as direct evidence for Selank.[1][3]

Human reports principally concern intranasal administration, while many mechanistic experiments use intraperitoneal dosing in rodents. Those routes create different absorption, concentration-time and tissue-distribution questions. Route is therefore part of the evidence identity.[1][2][4]

SECTION 20

GABA-related transcriptional programme

In rat frontal cortex, Selank and GABA produced correlated changes in expression of genes involved in neurotransmission. Forty-five genes changed one hour after administration and twenty-two at three hours in the reported experiment. This supports interaction with GABA-related regulatory networks without demonstrating direct benzodiazepine-site agonism.[2]

Gene-expression similarity is a mechanistic clue, not proof of identical pharmacology or clinical effect. Receptor binding, circuit function, behavioural output and human anxiety symptoms remain separate levels of inference.[2]

SECTION 21

Neurotrophic and immune-linked mechanisms

Rodent experiments have connected Selank with BDNF regulation, memory behaviour and monoaminergic balance under stress or injury models. These findings broaden the hypothesis beyond acute anxiolysis but remain preclinical and model dependent.[5]

Mouse spleen studies found changes in inflammation-related gene expression after Selank or its fragments, including time-dependent changes in C3, Casp1, Il2rg and Xcr1. This supports

immune-neural pleiotropy but does not identify a validated clinical immune indication.[4][6]

SECTION 22

Human anxiety signal

A comparative study enrolled 60 patients with phobic-anxiety, generalised-anxiety and somatoform diagnoses and reported anxiolytic and mild nootropic effects relative to phenazepam, with persistence after treatment. The indexed abstract does not fully resolve randomisation, allocation concealment, blinding or endpoint hierarchy.[1]

The report establishes a human clinical signal worth reproducing. It does not establish effect magnitude against modern comparators or placebo, does not define long-term recurrence and cannot support an injectable claim.[1]

SECTION 23

Human neurophysiology

A resting-state functional-connectivity study of 52 healthy participants examined Selank, Semax and placebo and reported changes involving the right amygdala and temporal regions. Imaging demonstrates a measurable neural response but is not a clinical anxiety endpoint.[7]

Small imaging experiments are sensitive to preprocessing, multiplicity and timing. They can refine circuit hypotheses and dose windows; they cannot establish durable symptom benefit, comparative efficacy or safety in a patient population.[7]

SECTION 24

Translation boundary

Selank has exact molecular identity, a coherent preclinical programme and limited human intranasal signals. Missing elements include route-specific PK, robust placebo-controlled outcomes, repeated-use safety and independent replication outside a concentrated research network.[1][2][7]

The correct conclusion is not that mechanism is absent. It is that the chain from sequence to human exposure to reproducible patient benefit remains incomplete. Each additional route constitutes a new pharmacological experiment.[1][2]

SECTION 25

Falsification map

Lack of reproducible GABA-related or neurophysiological response would weaken the proposed network.

Absent measurable intranasal exposure would force reinterpretation of the human signal.

No symptom benefit despite a replicated imaging response would falsify imaging-as-efficacy reasoning.

RESEARCH AGENDA

What would materially change the conclusion?

01 Human intranasal PK and bioavailability

02 Placebo-controlled anxiety trials with prespecified endpoints

03 Independent replication

04 Longitudinal tolerability and withdrawal assessment

05 Circuit-response correlation with symptoms

06 Separate parenteral exposure programme before injectable claims

CITED PRIMARY EVIDENCE CORPUS

8 source records

This corpus documents the claims made in this monograph; it is not presented as an exhaustive systematic-review search.

Medvedev et al. Zh Nevrol Psikiatr. 2014;114:17-22. · PMID 25176261

Uchakina et al. Zh Nevrol Psikiatr. 2008;108:71-75. · PMID 18577961

Andreeva et al. Inflammation-related gene expression in mouse spleen under Selank. Mol Immunol. 2011. · PMID 21609736

Panikratova et al. Functional connectomic approach to Selank and Semax effects. Dokl Biol Sci. 2020. · PMID 32342318

Volkova et al. Front Pharmacol. 2016;7:31. · PMID 26924987

Kolik et al. Selank regulates BDNF and memory effects in an ethanol-withdrawal rat model. Bull Exp Biol Med. 2019. · PMID 31625062

Kolomin et al. Temporal dynamics of inflammation-related genes under Selank. Peptides. 2013. · PMID 24291245

Zozulia et al. Efficacy and possible mechanisms of Selank in generalised anxiety disorder and neurasthenia. Zh Nevrol Psikiatr. 2008. Russian-language randomised comparative study. · PMID 18454096

AUTHORSHIP AND ACCOUNTABILITY

Valentine Wibowo performed the conceptualisation, evidence synthesis, scientific interpretation and drafting. dr. I Wayan Cahyadi Surya Distira Putra, MPH completed medical review and approved the publication. Internal medical review is not represented as independent journal peer review.

No new patient data or human research were undertaken. The author and reviewer declare no personal financial competing interests. Clinic Terrain and Klinik Pratama Cepat Sehat provide clinical services; that institutional relationship is disclosed.