

RESEARCH MONOGRAPH . COMPOUND PROFILE

FGL Peptide

A 15-residue synthetic peptide modeled on the second fibronectin-like domain of neural cell adhesion molecule, an FGFR1 partial agonist with neuroprotective and pro-cognitive activity in rodent models.

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ABSTRACT

FGL (FG Loop peptide; Glu-Val-Tyr-Val-Val-Ala-Glu-Asn-Gln-Gln-Gly-Lys-Ser-Lys-Ala; sometimes called the FGL peptide or NCAM-derived FGFR agonist; molecular weight approximately 1622 Da) is a synthetic 15-residue peptide modeled on the second fibronectin type III repeat (FnIII) domain of neural cell adhesion molecule (NCAM), specifically the Phe-Gly loop responsible for fibroblast growth factor receptor 1 (FGFR1) interaction. NCAM is a transmembrane glycoprotein expressed at high levels in developing and adult nervous system tissue that mediates cell-cell adhesion through homophilic NCAM-NCAM binding and signals across the membrane through cis-binding to FGFR1. The FGL peptide was designed at the University of Copenhagen by Elisabeth Bock and Vladimir Berezin as a small-molecule mimetic of the NCAM-FGFR interaction, capable of activating FGFR1 signaling without the broad effects of full NCAM ectodomain or full-length FGF ligands. Reported activities include neurite outgrowth promotion in primary cortical and hippocampal neurons, protection against glutamate excitotoxicity, anxiolysis and pro-cognitive effects in rodent fear conditioning and Morris water maze paradigms, and recovery promotion in models of traumatic brain injury and stroke. Routes studied include subcutaneous, intraperitoneal, and intranasal administration. Plasma half-life is short (approximately 30 minutes); the central nervous system exposure after intranasal administration is substantially higher than after parenteral routes, owing to direct olfactory and trigeminal pathway transport. The compound advanced through ENKAM Pharmaceuticals (a University of Copenhagen spin-out) into early clinical development for

Alzheimer's disease and cognitive impairment in the late 2000s; clinical development has not produced a marketed agent. The principal limitation on the strength of the evidence is the dominance of the originating laboratory's publications and the absence of independent replication of key behavioral findings.

1. Compound Identification

FGL Peptide is described as ncam-derived fgfr-agonist peptide. A 15-residue synthetic peptide modeled on the second fibronectin-like domain of neural cell adhesion molecule, an FGFR1 partial agonist with neuroprotective and pro-cognitive activity in rodent models.

1.1 Class summary

NCAM-derived FGFR-agonist peptide

1.2 Subtitle

A 15-residue synthetic peptide modeled on the second fibronectin-like domain of neural cell adhesion molecule, an FGFR1 partial agonist with neuroprotective and pro-cognitive activity in rodent models.

2. Abstract

FGL (FG Loop peptide; Glu-Val-Tyr-Val-Val-Ala-Glu-Asn-Gln-Gln-Gly-Lys-Ser-Lys-Ala; sometimes called the FGL peptide or NCAM-derived FGFR agonist; molecular weight approximately 1622 Da) is a synthetic 15-residue peptide modeled on the second fibronectin type III repeat (FnIII) domain of neural cell adhesion molecule (NCAM), specifically the Phe-Gly loop responsible for fibroblast growth factor receptor 1 (FGFR1) interaction. NCAM is a transmembrane glycoprotein expressed at high levels in developing and adult nervous system tissue that mediates cell-cell adhesion through homophilic NCAM-NCAM binding and signals across the membrane through cis-binding to FGFR1. The FGL peptide was designed at the University of Copenhagen by Elisabeth Bock and Vladimir Berezin as a small-molecule mimetic of the NCAM-FGFR interaction, capable of activating FGFR1 signaling without the broad effects of full NCAM ectodomain or full-length FGF ligands. Reported activities include neurite outgrowth promotion in primary cortical and hippocampal neurons, protection against glutamate excitotoxicity, anxiolysis and pro-cognitive effects in rodent fear conditioning and Morris water maze paradigms, and recovery promotion in models of traumatic brain injury and stroke. Routes studied include subcutaneous, intraperitoneal, and intranasal administration. Plasma half-life is short (approximately 30 minutes); the central nervous system exposure after intranasal administration is substantially higher than after parenteral routes, owing to direct olfactory and trigeminal pathway transport. The compound advanced through ENKAM Pharmaceuticals (a University of Copenhagen spin-out) into early clinical development for Alzheimer's disease and cognitive impairment in the late 2000s; clinical development has not produced a marketed agent. The principal limitation on the strength of the evidence is the dominance of the originating laboratory's publications and the absence of independent replication of key behavioral findings.

3. Mechanism of Action

FGFR1 partial agonist binding at the FnIII fibronectin-like domain interaction surface. Neurite outgrowth, anti-excitotoxic protection, and pro-cognitive effects in rodent models attributed to FGFR1-mediated MAPK and PI3K signaling.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

Rodent studies 1 to 8 mg/kg subcutaneous, intraperitoneal, or intranasal. Single-dose effects observed at 8 mg/kg.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Berezin V, Bock E. NCAM mimetic peptides: pharmacological and therapeutic potential. J Mol Neurosci 2004.
2. Cambon K, et al. A synthetic peptide ligand of NCAM with cognition-enhancing activity. J Neurosci 2004.
3. Secher T, et al. The FG loop peptide enhances cognitive function in rats. Neuroscience 2006.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.