Assembly and cell surface presentation of NMDA receptors

Bhattacharya, S., Camp, C., Martin, E.A., Miller, A.C., Orlic-Milacic, M., Traynelis, S.F.

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

16/11/2022
Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references


Reactome database release: 82

This document contains 1 pathway and 23 reactions (see Table of Contents)

https://reactome.org
Assembly and cell surface presentation of NMDA receptors

Stable identifier: R-HSA-9609736

N-methyl-D-aspartate receptors (NMDARs) are tetramers that consist of two GluN1 (GRIN1) subunits and two subunits that belong to either the GluN2 (GRIN2) subfamily (GluN2A, GluN2B, GluN2C and GluN2D) or the GluN3 (GRIN3) subfamily (GluN3A and GluN3B). The GluN2/GluN3 subunits in the NMDA tetramer can either be identical, constituting an NMDA di-heteromer (di-heterotetramer), which consists of two subunit types, GluN1 and one of GluN2s/GluN3s, or they can be two different GluN2/GluN3 proteins, constituting an NMDA tri-heteromer (tri-heterotetramer), which consists of three subunit types, GluN1 and two of GluN2s/GluN3s (Monyer et al. 1992, Wafford et al. 1993, Sheng et al. 1994, Dunah et al. 1998, Perez-Otano et al. 2001, Chatterton et al. 2002, Matsuda et al. 2002, Yamakura et al. 2005, Nilsson et al. 2007, Hansen et al. 2014, Kaiser et al. 2018, Bhattacharya et al. 2018, Bhattacharya and Traynelis 2018).

NMDA tetramers assemble in the endoplasmic reticulum and traffic to the plasma membrane as part of transport vesicles (McIlhinney et al. 1998, Perez-Otano et al. 2001). NMDA receptor subunits undergo N-glycosylation, which impacts their trafficking from the endoplasmic reticulum to the plasma membrane. Trafficking efficiency may vary among different subunits of NMDARs (Lichnereva et al. 2015). Mechanistic details, such as glycosyl transferases involved and the type of sugar side chains added, are not known.

As there are eight splicing isoforms of GluN1, four different GluN2 and two different GluN3 proteins, many different combinations of NMDAR subunits are possible, but only a handful of distinct NMDAR receptors have been experimentally confirmed and functionally studied. The composition of NMDARs affects trafficking, spatial (including synaptic) localization, ligand preference, channel conductivity and downstream signal transmission. Prevalent NMDARs differ at different stages of neuronal development, in different regions of the central nervous system, and at different levels of neuronal activity. For review, please refer to Lau and Zukin 2007, Traynelis et al. 2010, Paoletti et al. 2013, Pérez-Otaño et al. 2016, Iacobucci and Popescu 2017.

Literature references


**Editions**

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GluN2A (GRIN2A) forms a di-heterotetramer with GluN1 (GRIN1). Based on the crystal structure of the rat GluN1:GluN2A (Grin1:Grin2a) NMDA receptor (Furukawa et al. 2005) and the Cryo-EM structure of the human GluN1:GluN2A (GRIN1:GRIN2A) NMDA receptor (Zhang et al. 2018), the tetramer includes 2 molecules of GluN1 and two molecules of GluN2A. GluN2A expression starts postnatally and GluN2A is highly expressed in adult brain (Monyer et al. 1992, Sheng et al. 1994).

**Followed by:** GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors traffic to the plasma membrane

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Formation of di-heterotetramers of GluN1 (GRIN1) and GluN2B (GRIN2B)

Location: Assembly and cell surface presentation of NMDA receptors

Stable identifier: R-HSA-9609744

Type: binding

Compartments: endoplasmic reticulum membrane

Inferred from: Formation of di-heterotetramers of GluN1 and GluN2b (Rattus norvegicus)

GluN2B (GRIN2B) forms a di-heterotetramer with GluN1 (GRIN1). The tetramer includes two molecules of GluN1 and two molecules of GluN2B. GluN2B expression starts during embryonic development and continues in adult brain (Monyer et al. 1992, Sheng et al. 1994). The tetrameric structure is deduced from the crystal structure of the rat GluN1:GluN2B (Grin1:Grin2b) NMDA receptor (Karakas and Furukawa 2014) and the Xenopus GluN1:GluN2B NMDA receptor (Lee et al. 2014).

Followed by: GluN1:GluN2B (GRIN1:GRIN2B) di-heterotetramers bind LIN7:CASK:APBA1, DLG1 and KIF17

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Formation of di-heterotetramers of GluN1 (GRIN1) and GluN2C (GRIN2C)

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9609739

**Type:** binding

**Compartments:** endoplasmic reticulum membrane

**Inferred from:** Formation of di-heterotetramers of GluN1 (Grin1) and GluN2C (Grin2c) (Rattus norvegicus)

GluN1 (GRIN1) forms a di-heterotetrameric complex with GluN2C (GRIN2C) in heterologous expression systems. The tetramer includes two molecules of GluN1 and two molecules of GluN2C (Monyer et al. 1994). The stoichiometry in neurons remains to be determined. GluN2C expression starts late during embryonic development and is most prominent in cerebellum, olfactory bulb, and glial cells (Karavanova et al. 2007, Ravikrishnan et al. 2018, reviewed by Traynelis et al. 2010, Paoletti et al. 2013).

**Followed by:** GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors traffic to the plasma membrane

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Formation of di-heterotetramers of GluN1 (GRIN1) and GluN2D (GRIN2D)

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9609741

**Type:** binding

**Compartments:** endoplasmic reticulum membrane

**Inferred from:** Formation of di-heterotetramers of GluN1 (Grin1) and GluN2D (Grin2d) (Rattus norvegicus)

GluN1 (GRIN1) forms a di-heterotetramer with GluN2D (GRIN2D) in heterologous expression systems, although stoichiometry is unclear in neurons. The tetramer includes two molecules of GluN1 and two molecules of GluN2D (Dunah et al. 1998). GluN2D is expressed in the brain during embryonic development. In adult brain, GluN2D expression is low and mostly restricted to diencephalon and mesencephalon, as well as GABAergic interneurons (von Engelhardt et al. 2015, Perszyk et al. 2016, reviewed by Paoletti et al. 2013). The ligand binding domain of GluN2D interacts with agonists in a similar fashion to other GluN2 subunits (Vance et al. 2011, Hansen et al. 2013).

**Followed by:** GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors traffic to the plasma membrane

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Formation of di-heterotetramers of GluN1 (GRIN1) and GluN3A (GRIN3A)

Location: Assembly and cell surface presentation of NMDA receptors

Stable identifier: R-HSA-9609747

Type: binding

Compartments: endoplasmic reticulum membrane

Inferred from: Formation of di-heterotetramers of GluN1 (Grin1) and GluN3A (Grin3a) (Rattus norvegicus)

GluN3A (GRIN3A) interacts with GluN1 (GRIN1) to form a di-heteromeric NMDA receptor (Perez-Otano et al. 2001, Chatterton et al. 2002). The tetrameric structure of the GluN1:GluN3A (GRIN1:GRIN3A) di-heteromer is inferred from the tetrameric architecture of all known glutamate receptors (Traynelis et al. 2010). GluN3A expression reaches the highest level in early postnatal period and then declines (reviewed by Paoletti et al. 2013). GluN1:GluN3A di-heteromers can be activated by glycine in Xenopus oocytes (Smothers and Woodward 2007), and the action of glycine can be greatly enhanced by diminishing the ability of GluN1 subunit to interact with glycine (Awobuluyi et al. 2007, Kvist et al. 2013, Grand et al. 2018).
Formation of di-heterotetramers of GluN1 (GRIN1) and GluN3B (GRIN3B)

Location: Assembly and cell surface presentation of NMDA receptors

Stable identifier: R-HSA-9609728

Type: binding

Compartments: endoplasmic reticulum membrane

Inferred from: Formation of di-heterotetramers of GluN1 (Grin1) and GluN3B (Grin3b) (Rattus norvegicus)

GluN3B (GRIN3B) binds to GluN1 (GRIN1) to form a di-heteromeric NMDA receptor (Chatterton et al. 2002). The tetrameric structure of the GluN1:GluN3B (GRIN1:GRIN3B) di-heteromer is inferred from the tetrameric architecture of all known glutamate receptors (Traynelis et al. 2010). GluN3B expression gradually increases during development and is expressed at highest levels in the adult motor neurons (reviewed by Paoletti et al. 2013). GluN1:GluN3B (GRIN1:GRIN3B) di-heteromers can be activated by glycine in Xenopus oocytes but not in human embryonic kidney cell line HEK293 (Smothers and Woodward 2007).

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Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2A (GRIN2A) and GluN2B (GRIN2B)

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9609746

**Type:** binding

**Compartments:** endoplasmic reticulum membrane

**Inferred from:** Formation of tri-heterotetramers of GluN1 (Grin1), GluN2A (Grin2a) and GluN2B (Grin2b) (Rattus norvegicus)

GluN1 (GRIN1) forms a tri-heterotetramer with GluN2A (GRIN2A) and GluN2B (GRIN2B). The tetramer includes two molecules of GluN1, one molecule of GluN2A and one molecule of GluN2B (Sheng et al. 1994). The tetrameric structure of the GluN1:GluN2A:GluN2B (GRIN1:GRIN2A:GRIN2B) triheteromeric NMDA receptor was demonstrated on the cryo-EM structure of the Xenopus orthologue (Lu et al. 2017). The majority of native NMDA receptors in adult forebrain are GluN1:GluN2A:GluN2B tri-heteromers, and their pharmacological properties are distinct from the properties of GluN1:GluN2A and GluN1:GluN2B di-heteromers (Hansen et al. 2014).

**Followed by:** GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors traffic to the plasma membrane

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Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2A (GRIN2A) and GluN2C (GRIN2C)

Location: Assembly and cell surface presentation of NMDA receptors

Stable identifier: R-HSA-9609738

Type: binding

Compartments: endoplasmic reticulum membrane

Inferred from: Formation of tri-heterotetramers of GRIN1, Grin2a and Grin2c (Homo sapiens)

GluN1 (GRIN1) forms a tri-heterotetramer with GluN2A (GRIN2A) and GluN2C (GRIN2C). The tetramer includes two molecules of GluN1, one molecule of GluN2A and one molecule of GluN2C (Wafford et al. 1993). The tetrameric structure of the GluN1:GluN2A:GluN2C (GRIN1:GRIN2A:GRIN2C) tri-heteromer is assumed to be similar to the described structure of the Xenopus GluN1:GluN2A:GluN2B tri-heteromer (Lu et al. 2017). GluN1:GluN2A:GluN2C tri-heteromers are the predominant NMDA receptors in cerebellar granule cells (Bhattacharya et al. 2018, reviewed in Bhattacharya and Traynelis 2018).

Followed by: GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors traffic to the plasma membrane

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GluN1 (GRIN1) is assumed to form a tri-heterotetramer with GluN2A (GRIN2A) and GluN2D (GRIN2D). The tetramer includes two molecules of GluN1, one molecule of GluN2A and one molecule of GluN2D (Dunah et al. 1998). The tetrameric structure of the GluN1:GluN2A:GluN2D (GRIN1:GRIN2A:GRIN2D) tri-heterotetramer is assumed to follow from the cryo-EM structure of the triheteromeric Xenopus GluN1:GluN2A:GluN2B NMDA receptor (Lu et al. 2017).

**Followed by:** GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors traffic to the plasma membrane
Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2B (GRIN2B) and GluN2D (GRIN2D) ↗

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9609737

**Type:** binding

**Compartments:** endoplasmic reticulum membrane

**Inferred from:** Formation of tri-heterotetramers of GluN1 (Grin1), GluN2B (Grin2b) and GluN2D (Grin2d) (Rattus norvegicus)

GluN1 (GRIN1) binds GluN2B (GRIN2B) and GluN2D (GRIN2D) to form a tri-heteromeric NMDA receptor (Dunah et al. 1998). The tetrameric structure of the GluN1:GluN2B:GluN2D (GRIN1:GRIN2B:GRIN2D) tri-heterotetramer, consisting of two molecules of GluN1 (GRIN1) and one molecule of each GluN2B (GRIN2B) and GluN2D (GRIN2D), is assumed to be similar to the cryo-EM structure of the Xenopus GluN1:GluN2A:GluN2B NMDA receptor (Lu et al. 2017).

**Followed by:** GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors traffic to the plasma membrane

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Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2A (GRIN2A) and GluN3A (GRIN3A)

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9610270

**Type:** binding

**Compartments:** endoplasmic reticulum membrane

**Inferred from:** Formation of tri-heterotetramers of GluN1 (Grin1), GluN2A (Grin2a) and GluN3A (Grin3a) (Rattus norvegicus)

GluN1 (GRIN1) binds to GluN2A (GRIN2A) and GluN3A (GRIN3A) to form a tri-heteromeric GluN1:GluN2A:GluN3A (GRIN1:GRIN2A:GRIN3A) NMDA receptor (Perez-Otano et al. 2001, Nilsson et al. 2007, Tong et al. 2008).

**Literature references**


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Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2B (GRIN2B) and GluN3A (GRIN3A)

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9609743

**Type:** binding

**Compartments:** endoplasmic reticulum membrane

GluN1 (GRIN1) binds to GluN2B (GRIN2B) and GluN3A (GRIN3A) to form a tri-heteromeric NMDA receptor GluN1:GluN2B:GluN3A (GRIN1:GRIN2B:GRIN3A) (Das et al. 1998, Al-Hallaq et al. 2002, Nilsson et al. 2007).

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Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2B (GRIN2B) and GluN3B (GRIN3B)

Location: Assembly and cell surface presentation of NMDA receptors

Stable identifier: R-HSA-9609740

Type: binding

Compartments: endoplasmic reticulum membrane

Inferred from: Formation of tri-heterotetramers of GluN1 (Grin1), GluN2B (Grin2b) and GluN3B (Grin3b) (Mus musculus)

GluN1 (GRIN1) binds to GluN2B (GRIN2B) and GluN3B (GRIN3B) to form a tri-heteromeric NMDA receptor or GluN1:GluN2B:GluN3B (GRIN1:GRIN2B:GRIN3B) (Yamakura et al. 2005).

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**Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2A (GRIN2A) and GluN3B (GRIN3B)**

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9610327

**Type:** binding

**Compartments:** endoplasmic reticulum membrane

**Inferred from:** Formation of tri-heterotetramers of GluN1 (Grin1), GluN2A (Grin2a) and GluN3B (Grin3b) (Rattus norvegicus)

GluN1 (GRIN1) binds to GluN2B (GRIN2B) and GluN3B (GRIN3B) to form a tri-heteromeric NMDA receptor GluN1:GluN2B:GluN3B (GRIN1:GRIN2B:GRIN3B) (Yamakura et al. 2005).

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GluN1:GluN2B (GRIN1:GRIN2B) di-heterotetramers bind LIN7:CASK:APBA1, DLG1 and KIF17

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9610408

**Type:** binding

**Compartments:** endoplasmic reticulum membrane, transport vesicle membrane, cytosol

**Inferred from:** GluN1:GluN2B (Grin1:Grin2b) di-heterotetramers bind Lin7:Cask:Apba1 and Kif17 (Mus musculus), GluN1:GluN2B (Grin1:Grin2b) di-heterotetramers bind Dlg1 and Cask (Rattus norvegicus)

GluN1:GluN2B (GRIN1:GRIN2B) di-heteromers are transported to the plasma membrane from the endoplasmic reticulum (ER) via transport vesicles. At the membrane of transport vesicles, GluN1:GluN2B NMDA receptors associate with the complex of LIN7 (LIN7A, LIN7B or LIN7C), CASK and APBA1. The microtubule-associated kinesin motor protein KIF17 binds to the LIN7:CASK:APBA1 complex (Jo et al. 1999, Setou et al. 2000). During transport from ER to the plasma membrane, NMDA receptors are diverted from the somatic Golgi network and go through the dendritic ER subcompartment and dendritic Golgi instead. Besides CASK, interaction with DLG1 (SAP97) is required for GluN1:GluN2B NMDA receptors to go through this transport route (Jeyifous et al. 2009).

**Preceded by:** Formation of di-heterotetramers of GluN1 (GRIN1) and GluN2B (GRIN2B)

**Followed by:** KIF17 transports GluN1:GluN2B (GRIN1:GRIN2B) NMDA receptors to the plasma membrane

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https://reactome.org
KIF17 transports GluN1:GluN2B (GRIN1:GRIN2B) NMDA receptors to the plasma membrane

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9610627

**Type:** uncertain

**Compartments:** plasma membrane, transport vesicle membrane

**Inferred from:** Kif17 transports GluN1:GluN2 (Grin1:Grin2b) NMDA receptors to the plasma membrane (Mus musculus)

Kinesin KIF17 transports vesicles that contain GluN1:GluN2B (GRIN1:GRIN2B) NMDA receptor to the plasma membrane (Setou et al. 2000).

**Preceded by:** GluN1:GluN2B (GRIN1:GRIN2B) di-heterotetramers bind LIN7:CASK:APBA1, DLG1 and KIF17

**Followed by:** GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors bind to postsynaptic density proteins

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GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors traffic to the plasma membrane

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9610750

**Type:** uncertain

**Compartments:** endoplasmic reticulum membrane, plasma membrane

NMDA receptors composed of GluN1 (GRIN1) and various combinations of GluN2 (GRIN2) subunits (GluN2A, GluN2B, GluN2C and GluN2D) are all delivered to the plasma membrane where they are anchored to postsynaptic density regions via the interaction with the PSD-95 family of proteins (DLG1, DLG2, DLG3 and DLG3) (Cui et al. 2007). Details of trafficking from the endoplasmic reticulum to the plasma membrane for the majority of GluN1:GluN2 di-heteromers and tri-heteromers, except for GluN1:GluN2B NMDA receptors, are not known.

**Preceded by:**
- Formation of di-heterotetramers of GluN1 (GRIN1) and GluN2D (GRIN2D), Formation of di-heterotetramers of GluN1 (GRIN1) and GluN2A (GRIN2A), Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2B (GRIN2B) and GluN2D (GRIN2D), Formation of di-heterotetramers of GluN1 (GRIN1) and GluN2C (GRIN2C), Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2A (GRIN2A) and GluN2D (GRIN2D), Formation of tri-heterotetramers of GluN1 (GRIN1), GluN2A (GRIN2A) and GluN2B (GRIN2B)

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GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors bind to postsynaptic density proteins

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Location: Assembly and cell surface presentation of NMDA receptors

Stable identifier: R-HSA-9610653

Type: binding

Compartments: plasma membrane

Inferred from: GluN1 (Grin1) binds to Dlg4 (Rattus norvegicus)

All GluN2 (GRIN2) family subunits, GluN2A (GRIN2A), GluN2B (GRIN2B), GluN2C (GRIN2C) and GluN2D (GRIN2D), can bind to any of the PSD-95 protein family members DLG1 (SAP-97), DLG2 (PSD-93), DLG3 (SAP-102) and DLG4 (PSD-95). Binding to different PSD-95 family members does not affect transport of GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors to the plasma membrane, but does affect their positioning and retention at the plasma membrane postsynaptic density, as well as their excitability (Cui et al. 2007, Cousins et al. 2008, Bard et al. 2010). DLG4, the most prominent postsynaptic density protein, can also interact directly with GluN1 isoforms that possess the PDZ-binding domain in their C-terminus (Kornau et al. 1995).

Preceded by: KIF17 transports GluN1:GluN2B (GRIN1:GRIN2B) NMDA receptors to the plasma membrane

Followed by: GluN1 (GRIN1) binds to NEFL at postsynaptic density

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https://reactome.org
GluN1 (GRIN1) binds to NEFL at postsynaptic density

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9610879

**Type:** binding

**Compartments:** plasma membrane, cytosol

**Inferred from:** GluN1 (Grin1) binds Nefl (Rattus norvegicus)

The GluN1 (GRIN1) subunit of NMDA receptors binds to neurofilament light chain (NEFL, also known as NF-L), a type of cytoskeleton interfilaments, at postsynaptic density (PSD). Binding to NEFL may increase the stability of NMDA receptors at the PSD. Different GluN1 splicing isoforms may have different affinity for NEFL (Ehlers et al. 1998, Ratnam and Teichberg 2005). It is uncertain whether NEFL is a part of the core PSD (Dosemeci et al. 2007).

**Preceded by:** GluN1:GluN2 (GRIN1:GRIN2) NMDA receptors bind to postsynaptic density proteins

**Followed by:** GluN1 (GRIN1) binds to ACTN2 at postsynaptic density

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ACTN2 (alpha-actinin-2) directly binds to GluN1 (GRIN1) subunit of the NMDA receptor, but can also bind to GluN2B (GRIN2B) (Wyszynski et al. 1997). Binding to ACTN2 anchors NMDA receptors to the actin cytoskeleton and is needed for the assembly of the postsynaptic density (Wyszynski et al. 1997, Hodges et al. 2014).

**Preceded by:** GluN1 (GRIN1) binds to NEFL at postsynaptic density

**Followed by:** CaMKII and LRRC7 bind to NMDA receptors at postsynaptic density

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CaMKII and LRRC7 bind to NMDA receptors at postsynaptic density

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9611368

**Type:** binding

**Compartments:** plasma membrane, cytosol

**Inferred from:** CaMKII and Lrrc7 bind to NMDA receptors at postsynaptic density (Rattus norvegicus)

The calmodulin-dependent kinase, CaMKII, is enriched in postsynaptic density (PSD) and co-localizes with NMDA receptors. CaMKII can independently bind to alpha-actinin-2 (ACTN2), densin-180 (LRRC7) and the NMDA receptor subunit GluN2B (GRIN2B). Any of the four CAMK2 isoforms, CAMK2A, CAMK2B, CAMK2D or CAMK2G, which associate to form homomeric or heteromeric CaMKII dodecamers, can bind to ACTN2 and GluN2B, while LRRC7 shows the highest affinity for CAMK2A. Binding of CaMKII to the NMDA receptor-associated proteins is independent of CaMKII phosphorylation (Robison et al. 2005).

**Preceded by:** GluN1 (GRIN1) binds to ACTN2 at postsynaptic density

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GluN3A (GRIN3A), GluN3B (GRIN3B) NMDA receptors traffic to the plasma membrane

**Location:** Assembly and cell surface presentation of NMDA receptors

**Stable identifier:** R-HSA-9610802

**Type:** uncertain

**Compartments:** endoplasmic reticulum membrane, plasma membrane

**Inferred from:** GluN3A (Grin3a), GluN3B (Grin3b) NMDA receptors traffic to the plasma membrane (Rattus norvegicus)

NMDA receptors that contain GluN3A (GRIN3A) or GluN3B (GRIN3B) subunits, traffic to the plasma membrane to the perisynaptic regions, located at the periphery of the postsynaptic density (PSD). GluN3A and GluN3B do not have PDZ-binding domains and thus do not interact directly with PSD-95 family members. A small fraction of GluN3-containing NMDA receptors that localize to the central region of the PSD may be tri-heteromers with GluN2 (GRIN2) subunits (Perez-Otano et al. 2006, Wee et al. 2016).
NBEA binds DLG3

Location: Assembly and cell surface presentation of NMDA receptors

Stable identifier: R-HSA-9668218

Type: binding

Compartments: plasma membrane, cytosol

Inferred from: Nbea binds Dlg3 (Mus musculus)

Based on studies in mouse brain and cultured mouse neurons, NBEA (neurobeachin) forms a complex with DLG3 (SAP-102) (Lauks et al. 2012, Farzana et al. 2016). The PH domain in the C-terminus of NBEA is involved in this interaction (Lauks et al. 2012). Based on UniProt reference protein sequence alignment, human NBEA protein is 97% identical with mouse Nbea, while human DLG3 protein is 95% identical with mouse Dlg3.

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