Dorsal root ganglion connect to sensory neurons, allow distinguish the location and mode of stimulation.

Mechanoceptors: sense of pressure, made up of specialised ending sensory organs (e.g. Pacinian, Merkel receptors)

Nociceptors: senses tissue damaging stimulation (relatively higher threshold), e.g. heat cold chemical high pressure

- Mechanical nociceptor: MS
- TRP family receptors sense range of nociception, e.g. TRPV1: heat receptor, dectect spice

Processing of affarent signals: First point of integration in the spinal cord

- Aα and Aβ are myelinated mechanoceptors, project to the deeper lamina of the spinal cord
- Aδ (myelinated) and C fibre (unmyelinated) are nociceptors, project nociception to the superficial lamina of the spinal cord.

Early development of the mechanoceptive system: **develop before birth by testing reflexes in rats.**

Neural crest cells form the mechanoceptors an nociceptors following migration. **E9 in mice start formation**

- Mice sensory receptors develop in a rostral-caudal sequence
- Large mechanoceptor cells expressing TrkB and TrkC neutotrophin receptors develop before small nociceptive cells expressing TrkA

Specification of sensory neurons:

- Neural crest cells undergo first wave of lineage restriction with first set of transcription factor: Neurogenin I and II
  - Neurogenin I induce NCCs towards nociceptor fate
  - Neurogenin II induce NCCs towards mechanoceptor fate
- Second set of transcription factor further specifies the subtypes of sensory receptors: Runx I and III
  - Runx I specifies fate within nociceptors:
    - Maintained induction by Runx1 promote non-peptidergic cell fate (TrkA)
    - Transient induction by Runx1 promote peptidergic cell fate (TrkA)
  - Runx III specify fate within mechanoceptors
    - Maintained induction by Runx3 promote proprioceptor fate (TrkC)
    - Transient induction by Runx3 promote mechanoceptor fate (TrkB)
- Specified neurons with unique expression of Trk receptors migrate towards their target tissues expressing different neurotrophins.
  - NGF attract migration of nociceptors with TrkA
  - BDNF attract mechanoceptors with TrkB
  - Neurotrophin-3 attract proprioceptors with TrkC
- Glia-derived neurotrophic factor (GDNF) bind specificallt to the ret receptor expressed on NGNII+Runx3(transient) large a-cell mechanoceptors.

Development of sensory neurons: periphery vs central

- High specificity in peripheral sensory neurons, high neuronal growth followed by pruning, in the limb bud.
  - Immature machanoceptors have small receptive fields
  - poor functioning capacity
  - Poor frequency coding
- In mature mechanoceptors, a level of neurotrophin from skin tissue is required to maintain proper functioning of the neuron

- Sensitisation of nociceptors: expression of inflammatory substances reduce the firing threshold and firing frequency of peptidergic nociceptors.

- In the CNS, A-fibre project to deeper layers of the SC while C fibre project to the superficial layers
    - During development, the mechanosensory neurons project into the superficial and deep layers of the spinal cord
    - With tactile input during postnatal development, the superficial synapses are gradually pruned by microglia
    - Infections during pregnancy can lead to loss of microglia pruning dysfunction, may result in autism, anxiety disorder or schizophrenia.
    - **RFP labelling of mechanosensory neurons shows early innervation of superficial layers, which is then restricted into deeper layers**