2 Aims and overview of the present study.

2.1 Aims:

To find gene(s),

A. expressed in DRG neurons, which may also be involved in sensory mechanotransduction.

B. present in the extra-cellular region, which are associated with a mechanotransduction complex.

2.2 Overview:

It is known that different DRG neurons are responsible for sensing different types of mechanical stimuli. We hypothesized that if a gene expression is restricted to a subpopulation, then it may play a role in the detection of sensory stimuli detected by those neurons. NT3+/- mice and NT4-/- mice have lost specific subsets of sensory neurons. We hypothesized that NT3+/-// NT4-/- mice (NT34 mutant) would display a more profound functional loss than single mutants alone (Fig.05). In order to identify genes whose expression is altered in NT34 mutants, candidate transcripts obtained from gene chip experiments as well as genes obtained from an enriched cDNA library for regulated genes were used.

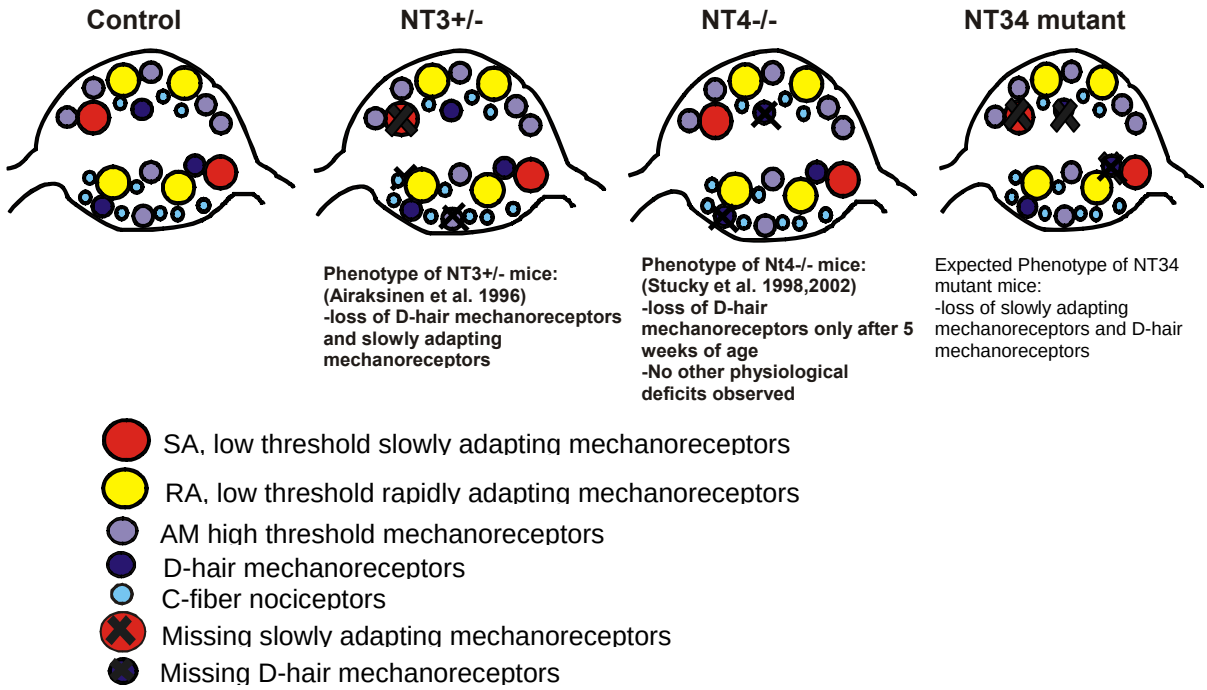

Fig. 05. Schematic diagram showing what is reported and the expected results.

Because of the specificity and reliability of *in situ* hybridization, we developed a high through put *in situ* hybridization method for our screening purpose. A subtracted cDNA library for the transcripts altered by BDNF was present in the lab. We were able to identify transcripts expressed in a subpopulation of DRG neurons and were able to verify them to have altered expression in BDNF+/- mice (BDNF mutant). In the second part of the studies, we were looking at the defects of NT34 mutant DRG neurons anatomically by electron microscopy, in the molecular level by gene chips as well as screening for enriched cDNA library for regulated transcripts and for the functional aspects using *in vitro* skin nerve recordings. These mice were also tested for tactile sensitivity. Third part of the study was carried out on SPP1-/- mice (SPP1 mutant). Secreted phophoprotein 1 / Osteopontin (OPN), was one of the genes found to have a subpopulation specific expression pattern. These mice were tested for defects using electrophysiological studies as well as behavioral studies for tactile sensitivity, heat sensitivity and tactile discrimination. The fourth part of the study was to identify extra cellular matrix proteins, which could bind to Acid sensing ion channel 3 (ASIC3), which was shown to play a role in sensory mechanotransduction. Overview of experiments is given in fig. 06.

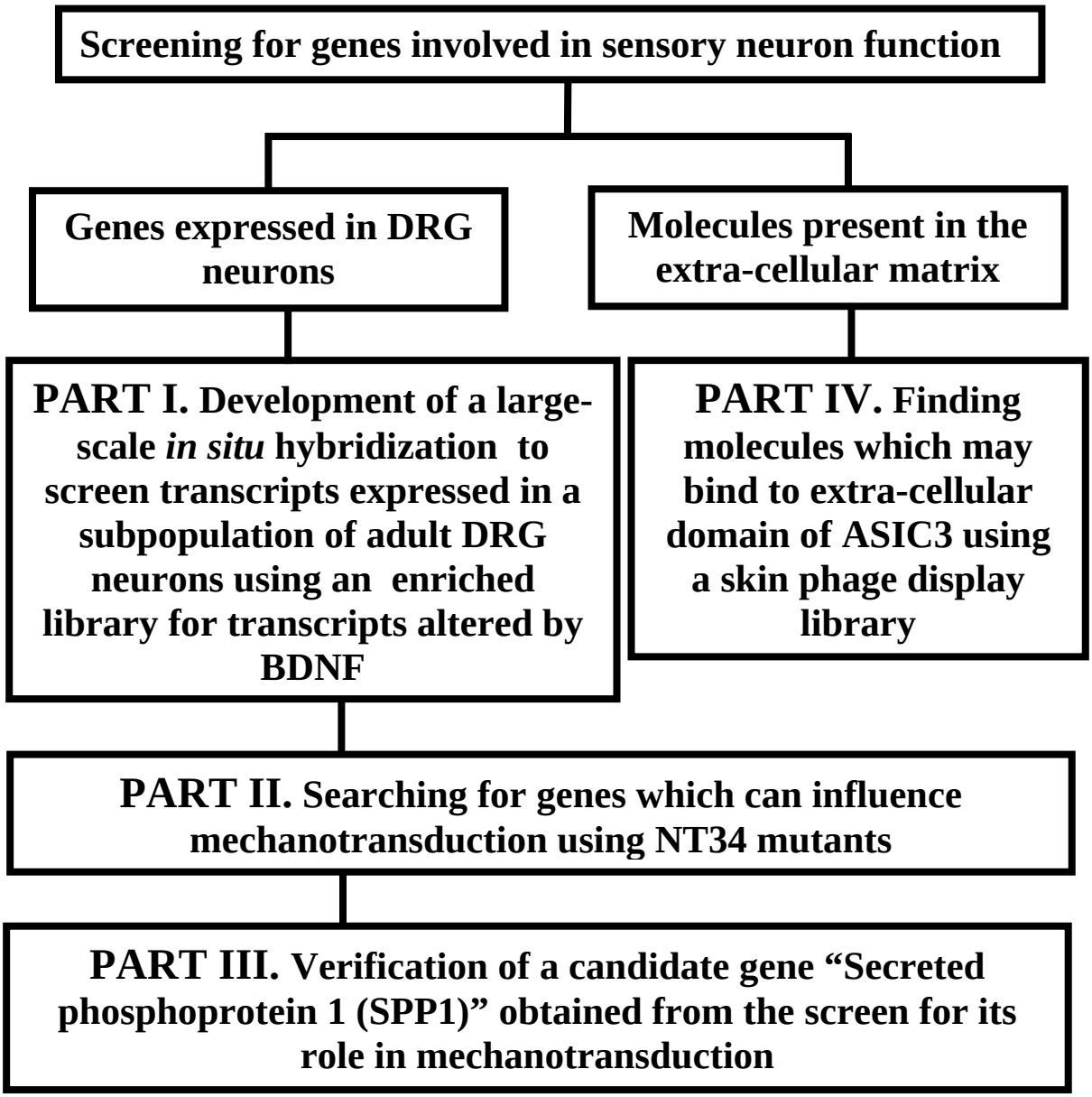

Fig. 06. Out line of all the experiments done