The enteric nervous system (ENS), located in the wall of the digestive tract and composed of millions of neurons, regulate all processes connected with intestinal activity, both under physiological conditions and during pathological states. It is well-known that enteric neurons are able to undergo structural, functional or chemical changes as a result of adaptive or reparative processes in response to physiological and pathological stimuli, such as development or aging, diet, nerve injury or intestinal and extra-intestinal diseases and the main symptom of these changes are alterations in the expression of neuronal active substances.

One of the less known substances, occurring in the enteric nervous system is neuregulin – 1 (NRG-1). In spite of relatively large number of studies on the presence of NRG-1 in various internal tissues and organs, the knowledge concerning the distribution and functions of this substance within the digestive tract is extremely scanty. Functions of neuregulin-1 in the enteric nervous system still remain unexplained and are pure conjecture. NRG-1 is expected to be a factor necessary for the proper development of the ENS during ontogenesis through participation in the growth and differentiation of enteric neurons. Probably neuregulin-1 in the ENS may play roles similar to those, which it plays in other parts of the nervous system, such as neuroprotective effects and the increase of survivability of neurons by the influence on Schwann cells.

The participation of NRG-1 in mechanisms connected with other pathological processes in the digestive tract has not been confirmed yet, but its neuroprotective activity as well as anti-inflammatory properties described in various parts of the nervous system strongly suggest similar roles in the ENS. Some previous studies have also described that NRG-1 may take part in the pathological processes within the digestive tract, especially in these, which are characterized by atrophy of enteric nervous structures, including Hirschsprung's disease, diverticulosis, slow-transit constipation or gastrointestinal neuromuscular diseases.

The planned investigation will enrich the existing knowledge concerning distribution and functions of NRG-1 within the large intestine not only in physiological conditions, but also after administration of bisphenol A (BPA). BPA is one of the most widespread toxin in the human environment. It is commonly used in the production of plastic, including bottles, food containers toys and other everyday objects. BPA may penetrate the food and water and has multidirectional negative effects on the living organism. BPA influences on the reproductive, nervous, gastrointestinal, endocrine and immune systems. It is also known that exposition to BPA results in diabetes, obesity and/or hypertension. Previous studies have shown that the first subclinical symptoms of intoxication with BPA are changes in neurochemical characterization of the enteric neurons, but till now the functions of NRG-1 in the enteric neurons under the impact of BPA have not been studied.

The aim of planned study will be the determination of distribution of NRG-1 within neuronal cells of the enteric nervous system (ENS) and intramural colonic nerves in the selected parts of the large intestine, as well as investigation on the co-localization of NRG -1 with other, better known, neuronal active substances within enteric neurons, including galanin (GAL), choline acetylotransferase (ChAT - marker of cholinergic neurons), neuronal form of nitric oxide synthase (nNOS - marker of nitrergic neurons), substance P (SP) and vasoactive intestinal polypeptide (VIP). Moreover, the influence of low and high doses of BPA on the number and chemical coding of neurons and nerves, which show the presence of NRG-1 will be also studied. Standard and generally accepted in laboratories all over the world methods (such as double and single immunofluorescence technique) will be used during the planned investigation.

Innovative character of the project emphasizes by the fact, that till now the knowledge concerned the distribution and functions of NRG-1 within the enteric nervous system is rather scanty.

Moreover, the selection of the domestic pig as an experimental animal during planned investigations is not accidental. Due to some similarities between human and pig in the construction of digestive tract as well as its reactions on pathological states, the pig is often used as experimental model (better than commonly used rodents) in studies on the influence of various factors on the human digestive tract. So, the results obtained during planned investigations will be a started point to formulation of animal model of expression, distribution and roles of NRG 1 in the human gastrointestinal tract in physiological conditions and during intoxication with BPA.