CHAPTER VI: Future Directions

1 Thymulin and the Thymus-Pituitary Axis

The studies reviewed in previous chapters point to thymulin as a hypophysiotropic molecule which plays a physiologic role in the communication between the thymus and the pituitary gland, particularly during early life. The availability of antibodies from different species against FTS will facilitate the pursuit of *in vitro* and *in vivo* studies aimed at further understanding the mechanisms by which thymulin influences neuroendocrine function. In turn, these studies may lead to the utilization of thymulin to restore thymic endocrine function in clinical situations associated with thymus deficiency, like aging and chronic stress.

2 Antiinflammatory Thymulin Gene Therapy in the Brain

Chronic brain inflammation is thought to be a potential cause of nigral dopaminergic neurodegeneration in Parkinson´s disease (McGeer and McGeer 2004). In this context, it is of interest to search for antiinflammatory molecules which are active in the brain and can be used in long-term treatments aimed at protecting nigral neurons from the deleterious effects of pro-inflammatory agents. Thymulin is emerging as a promising candidate to fulfill such requirements. Thus, thymulin is an immunomodulatory peptide (Safieh-Garabedian, Kendall et al. 1992) which has been used in the past for the treatment of certain autoimmune pathologies (Bach 1984). As already mentioned, recent studies suggest that thymulin possesses antiinflammatory activity in the CNS (Safieh-Garabedian, Dardenne et al. 2002; Safieh-Garabedian, Ochoa-Chaar et al. 2003). Interestingly, an adenoviral vector harboring a synthetic gene for the thymulin analog metFTS has recently been constructed and shown to induce long-term expression of transgenic thymulin in serum when i.m. injected in mice and rats (Reggiani, Herenu et al. 2006). Furthermore, stereotaxic injection of the above adenoviral vector in the susbstantia nigra of rats elicited long-term expression of transgenic thymulin in this brain region (Morel, Brown et al. 2006). In this context, thymulin appears as a potentially suitable therapeutic tool for the amelioration of pathologies involving chronic brain inflammation.