PREFACE

Recent advance in molecular biology revealed new insights into the function of insulin receptor signaling and insulin receptor substrate (IRS) protein mediated signals in the central nervous system (CNS) *in vivo*. The IRS protein family contains at least four members, IRS-1 to IRS-4. IRS-1, -2 and -4 are expressed in the mammalian CNS. The IRS proteins mediate mainly intracellular effects of the insulin-like growth factor-1 receptor (IGF-1R) and the insulin receptor (IR). The functions of IRS proteins in peripheral tissues like muscle, liver, pancreas, and fat have been characterized in detail. However, much less is known about the role of IRS protein mediated signals in the CNS. Research on conventional and conditional knockout mice partially revealed the role of IRS signaling in the CNS. Recent data demonstrate an important function of IRS protein expression for neuronal proliferation and timing of myelination during brain development. In the hypothalamus, IR/IRS-2 mediated signals regulate reproduction and energy homeostasis. Moreover, IRS protein expression in the CNS influences life span in flies and rodents, suggesting that cerebral IRS signaling is a key regulator not only for brain development but also for aging. The IR and IGF-1R as well as IRS proteins might play an important role in the pathogenesis of neurodegenerative diseases. In particular, in Alzheimer's disease expression of neuronal IRs, IGF-1Rs, and IRS-1/-2 proteins is decreased. Interestingly, these changes in protein expression accelerate with severity of neurodegeneration, raising the question whether decreased IR, IGF-1R and IRS-1/-2 expression is cause or consequence of neurodegeneration. Thus, IRS signaling is not only critical during brain development but also for reproduction, energy homeostasis, as well as aging and possibly for neurodegenerative diseases in humans.