was that of whether melatonin would influence the expression of SIRT1. Reports concerning melatonin effects on SIRT1 levels demonstrated strongly contrasting changes of either down- or up-regulations. However, the conditionality of this divergence became readily obvious. When studied in melatonin-responsive cancer cells or tissues, in which apoptosis is induced by this agent, melatonin consistently caused a suppression of SIRT1.[55–57] However, in other systems, the opposite was observed. Melatonin up-regulated SIRT1 in various models of brain injury,[58–61] in myocardial ischemia-reperfusion,[62] in mesenchymal stem cells,[63,64] and, notably, in senescence-accelerated, normally aged, old ovariectomized rodents or in cultured neurons from old animals.[27,65–72] The discrepancy between tumour and non-tumour cells is explained by differences in the circadian oscillator system.[73] In tumour cells, cellular circadian oscillators are strongly dysregulated by epigenetic silencing of several core oscillator genes, especially *Per2*, which otherwise have tumour suppressor properties. Apart from this necessity for being able to exist as a tumour cell, the silencing seems to fix the oscillators in positions favouring cell proliferation, which are characterized by high expression levels of SIRT1 and CLOCK. Melatonin strongly reduces the expression of these two proteins and, thus, proliferative capacity.[73] *Via* further signalling connections, it also allows and promotes apoptosis, which is otherwise inhibited by melatonin in non-tumour cells.[5] In well-operating oscillators, melatonin can only act phase-dependently. Aging-related reductions in the expression levels of SIRT1 and also the core oscillator proteins PER2 and BMAL1 can be reversed by the pineal hormone.[73] In the gerontological context, up-regulation of SIRT1 was accompanied by corresponding changes in acetylated substrates and components of the downstream signalling pathways.[11] These data as well as the changes in interrelated and converging pathways have been summarized in a recent review.[11] These include signalling by NO, peroxisome proliferator-activated receptor-γ coactivator-1α (PGC-1α), peroxisome proliferator-activated receptor-γ (PPARγ), LKB1 (liver kinase B1), PI3K and Akt/PKB. Moreover, it should be briefly mentioned that research has now started to also consider effects of melatonin on other members of the seven mammalian sirtuins. SIRT2 was reported to be increased by melatonin in the aging colonic mucosa.[74] In the dentate gyrus of aging rats, the senescence-dependent decrease of SIRT2 was reversed by growth hormone, but not by melatonin, contrary to stimulatory effects on SIRT1.[70] In hepatocytes, melatonin was shown to up-regulate SIRT3, one of the sirtuins located in mitochondria, in conjunction with elevations of MnSOD, the superoxide dismutase subform of this organelle.[75] The inductions of SIRT3 and MnSOD were also reported to be prevented by knockdown of AMPK,[75] a finding that raises new questions concerning the divergent results on the relationship between melatonin and this kinase. In the context of hepatic cadmium toxicity, another study described melatonin-induced increases in SIRT3 activity, but not SIRT3 expression, along with reduced MnSOD acetylation, *i.e.*, activation of this enzyme, and suppression of autophagic cell death.[76] Further systematic investigation of all sirtuin subforms may be a promising field of future melatonin research.