CHAPTER ONE

AIMS OF THE STUDIES

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Chapter 2:	Introduction; to summarize the evidence for the chemopreventative efficacy of statins, with emphasis on their proposed molecular mechanism(s) of action and their potential for individualized use in chemoprevention.
Chapter 3:	To investigate whether the influence of statin use on the risk of developing colorectal cancer is dependent on the expression of SMAD4 in the tumor, or on the presence of *K-ras* and *BRAF* mutations in a large patient cohort.
Chapter 4:	To investigate whether nuclear pSMAD2,3 or pSMAD1,5,8 expression, biomarkers for the activity of the BMP and TGF- β pathways, can be used as a prognostic markers in CRC and to compare this with the prognostic value of SMAD4.
Chapter 5:	To assess the influence of statins on global cell signaling in a hypothesis-free manner.
Chapter 6:	To investigate whether statin treatment influences the methylation status of the *BMP2* promoter. To investigate whether the effects of statins have potential clinical application by modifying CRC chemosensitivity.
Chapter 7:	To investigate the effect of statin treatment on the expression and localization of the BMP receptors, changes in Caveolin and Clathrin expression and the balance between canonical and non-canonical BMP signaling in colorectal cancer cells.
Chapter 8:	To investigate the role of EZH2 and RUNX3 in sporadic CRCs and CRC cell lines and specifically whether EZH2 mediated chromatin changes are responsible for RUNX3 gene silencing and therefore represent a new mechanism of tumor suppressor loss.