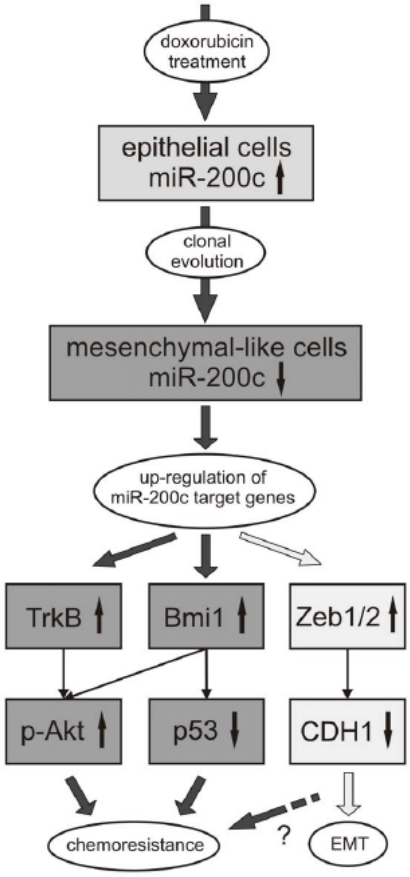
miRNAs involved in chemoresistance

In this project we determine the contribution of different miRNAs to chemoresistance. A previous publication of our group demonstrated the involvement of miRNA-200c in doxorubicin- induced resistance (Kopp *et al*.).
Treatment of epithelial cells expressing miR-200c with doxorubicin leads to clonal evolution of miR-200c low expressing and mesenchymal-like cells. In consequence, a variety of miR-200c target genes are upregulated. Besides the induction of EMT by the up-regulation of the ECadherin (CDH1) repressors Zeb1 and Zeb2, the loss of miR-200c expression can cause an elevation of resistance factors like TrkB and Bmi1 resulting in enhanced cell survival. This leads to the activation of anti-apoptotic pathways like the phosphorylation of Akt or the degradation of p53 which can be further modulated by a complex crosstalk.



Model of miR-200c regulated chemoresistance.