

Progress Report for the project  
“Molecular basis of tumor formation by pathogenic bacteria”  
supported by a Misrock Foundation Fellowship for the Ph.D. student Florine Scheidegger

Responsible investigator und thesis supervisor: Prof. Christoph Dehio

Reporting period: April 16<sup>th</sup>, 2008 to December 15<sup>th</sup>, 2008

Florine Scheidegger started her PhD project “Molecular basis of tumor formation by pathogenic bacteria” on November 1<sup>st</sup> 2004. The reporting period of eight month thus covers the progress from approximately year 3½ to year to the end of the PhD thesis in December 2008. In this reporting period, Ms. Scheidegger has successfully applied an *in vitro* model of human vascular tumor formation in response to infection with the tumor-inducing pathogen *Bartonella henselae* that she had established during the previous reporting period.

Ms. Scheidegger was using this *in vitro* model of vascularization to systematically explore the role of seven bacterial effector proteins (BepA-BepG) injected by *B. henselae* into human cells in the process of infection-triggered vascular tumor formation. Ms. Scheidegger could demonstrate that the different bacterial effector proteins have distinct effects on vascular proliferation. Most remarkably, the effector BepA (previously characterized as a cell death-inhibiting protein in the first publication by Ms. Scheidegger) has a marked stimulatory effect on vascularization, while adversely the effector BepG inhibits vascularization. Ms. Scheidegger has also shown that the cocktail of all seven bacterial effectors (BepA-BepG) prominently stimulates vascularization, while at the same time the infected cells do not respond anymore to vascular endothelial growth factor (VEGF), an important human growth factor for the stimulation of physiological and pathological vascularization. In the course of these studies, Ms. Scheidegger has been able to work out important aspects of the signaling processes triggering vascularization in the infected human endothelial cells, in particular the role of signaling by intracellular Calcium ions. A major part of these data have meanwhile been published in an internationally well recognized original research paper (Scheidegger et al., 2009, Distinct activities of *Bartonella henselae* type IV secretion effector proteins modulate capillary-like sprout formation. Cell. Microbiol. 11, 1088-1101). This publication also composes a major part of her Ph.D. thesis which she successfully defended on December 15<sup>th</sup>, 2008 with the grade “*cum laude*”.

Taken together, during the last reporting period Florine Scheidegger has made important progress in her Ph.D. project resulting in the publication of a second original research paper and the successful defense of her PhD thesis. Once more I like to thank the Misrock Foundation for funding Ms. Scheidegger as a Ph.D. student in my laboratory.

Basel, 17<sup>th</sup> January 2009



Prof. Christoph Dehio (Ph.D.)