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EDITORIAL

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Editorial foreword: Angiogenesis: Cells, tissues and organs

On the occasion of his 90th birthday, this Special Issue is dedicated to Professor Robert Auerbach. Born 1929 in Berlin, Germany, he and his family escaped Nazi Germany in 1939 and emigrated to the United States, where he became a zoologist and ultimately Professor and Director of the Developmental Biology Training Program at the Department of Zoology, Madison, University of Wisconsin, USA. In Auerbach's laboratory, students and scientists of many different nations, including politically persecuted ones, harmoniously worked together on different aspects of angiogenesis. One of the hallmarks of Auerbach's career as a scientist was and is his generosity towards others, sharing his equipment and ideas freely, his integrity and his collegiality. His significant contributions to angiogenesis and tumour research include the finding that angiogenesis in tumours can occur even after their irradiation (Auerbach, Arensman, Kubai, & Folkman, 1975) and an explanation of organ selectivity in the spread of metastasizing cancer cells (Auerbach, 1988). Through his outstanding papers on in vitro methods in angiogenesis research, he also supported animal welfare (Alby & Auerbach, 1984; Auerbach, Lewis, Shinners, Kubai, & Akhtar, 2003; Gumkowski, Kaminska, Kaminski, Morrissey, & Auerbach, 1987; Obeso, Weber, & Auerbach, 1990).

Angiogenesis, the sprouting of new blood vessels from pre-existing ones, is essential in prenatal development, growth and repair, but also contributes to pathological processes. In the healthy adult, it plays a significant role in the female ovulation cycle and in pregnancy, hair growth, exercise-induced growth of skeletal muscle and wound repair (Carmeliet, 2003; Olfert, Baum, Hellsten, & Egginton, 2016). There are only a few locations in the healthy body devoid of blood vessels such as the epidermis, cartilage, as well as the lens and cornea of the eye. In these organs and tissues, angiogenesis occurs only under pathological situations; for example, angiogenesis in hyaline cartilage is a characteristic of osteoarthritic joints (Bonnet & Walsh, 2005). However, it is its fundamental role in cancer growth and metastasis that has led to the tremendous interest in angiogenesis.

Current research on angiogenesis began in the 1970s when Judah Folkman (1933–2008) hypothesized that the growth of tumours is dependent on angiogenesis. He postulated that in order to survive and grow, tumours require blood vessels, and that by cutting off that blood supply, cancer could be starved into remission (Ribatti, 2008; Folkman, 1971). In 1975, Robert Auerbach, who worked with Folkman, grafted gamma-irradiated tumour cells into the chicken chorioallantoic membrane as well as into the cornea of adult rabbits. These experiments demonstrated that tumour-induced angiogenesis can occur even after their irradiation and led to the statement: "Our results provide additional support for the notion that tumour angiogenesis may be quite unique and that the approach to tumour control by interference with angiogenesis may well be a profitable one." Auerbach, Folkman and colleagues published their pioneering work in 1975 (Auerbach et al., 1975) and thus inaugurated a new era of intensive research into angiogenesis (McCain & Salter, 2007) based on the idea that anti-angiogenesis may be a method to control the growth of a tumour.

Subsequently, many cellular and molecular mechanisms involved in angiogenesis in health and disease have been identified (D'Alessio, Moccia, Li, Micera, & Kyriakides, 2015). Additionally, new therapeutic strategies have been developed based upon pro- and anti-angiogenesis for a variety of diseases, including some forms of cancer.

However, even with all its successes, there have been scenarios where angiogenesis research has not lived up to the high expectations placed upon it; for example, anti-angiogenic tumour therapy has not been as successful as initially hoped. One reason for this is that alternate mechanisms of neovascularization such as vascular

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mimicry exist (Ge & Luo, 2018). For example, vascular mimicry is utilized by highly aggressive cancer cells as found in glioblastomas to generate vascular-like structures promoting tumour growth (Angara, Borin, & Arbab, 2017). The role of vascular mimicry in tumour progression still needs to be studied in more detail in order to translate new findings into therapeutic strategies.

Apart from journals specialized on the topic of angiogenesis like "Angiogenesis," over the past years, several special issues in prominent international fora have been devoted to angiogenesis research. For example, the journal "Investigational New Drugs" published a special issue on "Development of angiogenesis inhibitors for cancer therapy" in 1997 (Volume 15, Issue 1, 1997 ISSN: 0167-6997). "Cancer Letters" circulated a special issue on "Angiogenesis-convergent or divergent, that is the question: Research toward targeted strategies in oncology" (Cai, 2016).

More recently, a special issue of the journal "BioMed Research International" highlighted "The Role of Endothelium in Physiological and Pathological States" (Stanek, Fazeli, Bartuś, & Sutkowska, 2018).

The present special issue presents the results and views of scientists working in the fields of veterinary anatomy, histology and embryology on "Angiogenesis: Cells, Tissues and Organs." I would like to sincerely thank all colleagues who supported this issue with their contributions.

Johanna Plendl

Department of Veterinary Medicine, Institute of Veterinary Anatomy, Freie Universitaet Berlin, Berlin, Germany
Email: *Johanna.Plendl@fu-berlin.de*

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