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# Regulation of red cell life-span, erythropoiesis, senescence, and clearance

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The number of red blood cells (RBCs) and their properties are optimized by nature for most efficient oxygen delivery from the lungs to hypoxic periphery. Changes in metabolic requirements or environmental oxygen availability quickly translate to modulation of the RBC number, blood rheology, oxygen affinity of hemoglobin, and even of vascular tone. Inability to match the changes in oxygen demand may be fatal and requires therapeutic intervention. The recent advances in the ongoing intensive investigations of the mechanisms in control of regulation of erythropoiesis, RBC maturation and aging, as well as the processes involved in recognition of senescent RBCs and their clearance make up the present volume.

It all starts from within the mesoderm, the fetal liver and from the adult bone marrow where primitive or definitive erythropoiesis takes place (Palis, 2014). Facilitated RBC production may be induced promptly “on demand” in extended oxygen requirements upon ascent to the high altitude and quickly reversed when extra RBC mass is without benefit any more (Risso et al., 2014). Exercise and professional sport increase RBC turnover and maximize oxygen delivery to the tissues (Mairbäurl, 2013). Maturation and aging of RBCs is accompanied by multiple processes occurring at various rates driving the circulating RBCs from adolescence to senescence within approximately 120 days (Lew and Tiffert, 2013; Lutz and Bogdanova, 2013). The resulting “markers of senescence” are recognized by the macrophages and clearance of RBCs is promptly initiated (de Back et al., 2014). Premature clearance is a hallmark of various disorders associated with anemia. In each case one or multiple markers of senescence appear prematurely. Those include excessive oxidative stress (Mohanty et al., 2014), excessive cation leak with the following dehydration (Wang et al., 2014), decrease in RBC size and loss of RBC membrane through vesiculation (Alaarg et al., 2013), metabolic abnormalities (Vives-Corróns et al., 2013), or following autoimmune diseases (Lutz and Bogdanova, 2013). Blood storage damages RBCs facilitating aging. As a result clearance of transfused cells is dramatically facilitated (Bosman, 2013; Flatt et al., 2014).

The present compilation does not only give an overview of the variety of opinions reflecting the current understanding of the mechanisms of erythropoiesis, aging, and clearance of RBCs. We hope that it also provides the base for future lively discussions of the up-standing problems in this rapidly developing research area.

## REFERENCES

- Alaarg, A., Schiffelers, R. M., van Solinge, W. W., and van Wijk, R. (2013). Red blood cell vesiculation in hereditary hemolytic anemia. *Front. Physiol.* 4:365. doi: 10.3389/fphys.2013.00365
- Bosman, G. J. C. G. M. (2013). Survival of red blood cells after transfusion: processes and consequences. *Front. Physiol.* 4:376. doi: 10.3389/fphys.2013.00376
- de Back, D. Z., Kostova, E. B., van Kraaij, M., van den Berg, T. K., and van Bruggen, R. (2014). Of macrophages and red blood cells; a complex love story. *Front. Physiol.* 5:9. doi: 10.3389/fphys.2014.00009
- Flatt, J. F., Bawazir, W. M., and Bruce, L. J. (2014). The involvement of cation leaks in the storage lesion of red blood cells. *Front. Physiol.* 5:214. doi: 10.3389/fphys.2014.00214
- Lew, V. L., and Tiffert, T. (2013). The terminal density reversal phenomenon of aging human red blood cells. *Front. Physiol.* 4:171. doi: 10.3389/fphys.2013.00171
- Lutz, H. U., and Bogdanova, A. (2013). Mechanisms tagging senescent red blood cells for clearance in healthy humans. *Front. Physiol.* 4:387. doi: 10.3389/fphys.2013.00387
- Mairbäurl, H. (2013). Red blood cells in sports: effects of exercise and training on oxygen supply by red blood cells. *Front. Physiol.* 4:332. doi: 10.3389/fphys.2013.00332
- Mohanty, J. G., Nagababu, E., and Rifkind, J. M. (2014). Red blood cell oxidative stress impairs oxygen delivery and induces red blood cell aging. *Front. Physiol.* 5:84. doi: 10.3389/fphys.2014.00084
- Palis, J. (2014). Primitive and definitive erythropoiesis in mammals. *Front. Physiol.* 5:3. doi: 10.3389/fphys.2014.00003
- Risso, A., Ciana, A., Achilli, C., Antonutto, G., and Minetti, G. (2014). Neocytolysis: none, one or many? A reappraisal and future perspectives. *Front. Physiol.* 5:54. doi: 10.3389/fphys.2014.00054
- Vives-Corróns, J.-L., Koralkova, P., Grau, J. M., Mañú Pereira, M. D. M., and van Wijk, R. (2013). First description of phosphofructokinase deficiency in Spain: identification of a novel homozygous missense mutation in the PFKM gene. *Front. Physiol.* 4:393. doi: 10.3389/fphys.2013.00393
- Wang, J., van Bentum, K., Sester, U., and Kaestner, L. (2014). Calcium homeostasis in red blood cells of dialysis patients in dependence of erythropoietin treatment. *Front. Physiol.* 5:16. doi: 10.3389/fphys.2014.00016

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