Editorial

Non-Haematological Effects of Erythropoietin

The involvement of a humoral factor (named as haemopoietin) in the regulation of haematopoiesis, was firstly described in literature in 1906 [1]. A link between erythropoietin (EPO) and erythropoiesis was described 40 years later [2], and in 1950s it was established that the kidney is the main site of production of EPO [3]. In 1977, EPO was purified from urine collected from patients suffering from aplastic anaemia [4], the nucleotide sequence of human EPO gene was determined in 1985 and the cloning and expression of the gene led to the production of recombinant human EPO (rhEPO) [5, 6]. The first clinical trial using rhEPO in the treatment of the anaemia of end-stage renal failure was published in 1987 [7]. Since then, many therapeutic trials have been developed to demonstrate the potential use of rhEPO in the treatment of different kinds of anaemia, namely associated with prematurity, AIDS, malignancies, congestive heart failure, post chemotherapy and post transplantation [8].

More recently, a wide distribution of EPO receptor (EPOR) expression in body cells and tissues was demonstrated [9]. For this reason, it is expected that EPO may have functions outside the erythroid cells. An increasingly growing body of evidence indicates that therapeutic benefits of rhEPO could be far beyond correction of anaemia, including renal, cardiovascular, immune and nervous systems protection/regeneration.

However, more investigation on this subject will be required. In fact, the majority of the works on this subject have been performed in animal models, by using intraperitoneal administration of high rhEPO doses, although usually as a single dose. rhEPO also induces a dose-dependent increase of blood pressure and increase the risk of thrombosis. Furthermore, it will be recognised that EPO receptors were also present in several tumours "*in vivo*", as well as in tumour lines, which led to debate on the possibility of adverse effects of EPO in malignancy patients. By these reasons, robust clinical trials will be required for a better determination of the effective risk-benefits of rhEPO treatment, and also the doses required for rhEPO treatment in these novel clinical areas.

In this special supplement of "*The Open Drug Discovery Journal*", four reviewers papers have been included; two of them on renal tissue effect of EPO [10, 11], one on the application of EPO in neurodegenerative disorders [12] and another about the levels of EPO in cardiac resynchronisation patients [13]. Finally, this supplement include an original article [14] that intend to study the effect of rhEPO on inflammation, oxidative stress and renal function/renoprotection, by using a rat model of moderate renal failure. We hope that this supplement could be useful to stimulate more research in this area, particularly concerning to robust clinical trials in non-anaemic patients.

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