Erythropoietin: Genetics, Control, Action and Clinical Applications

Review of Literature
Submitted for Partial Fulfillment
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By

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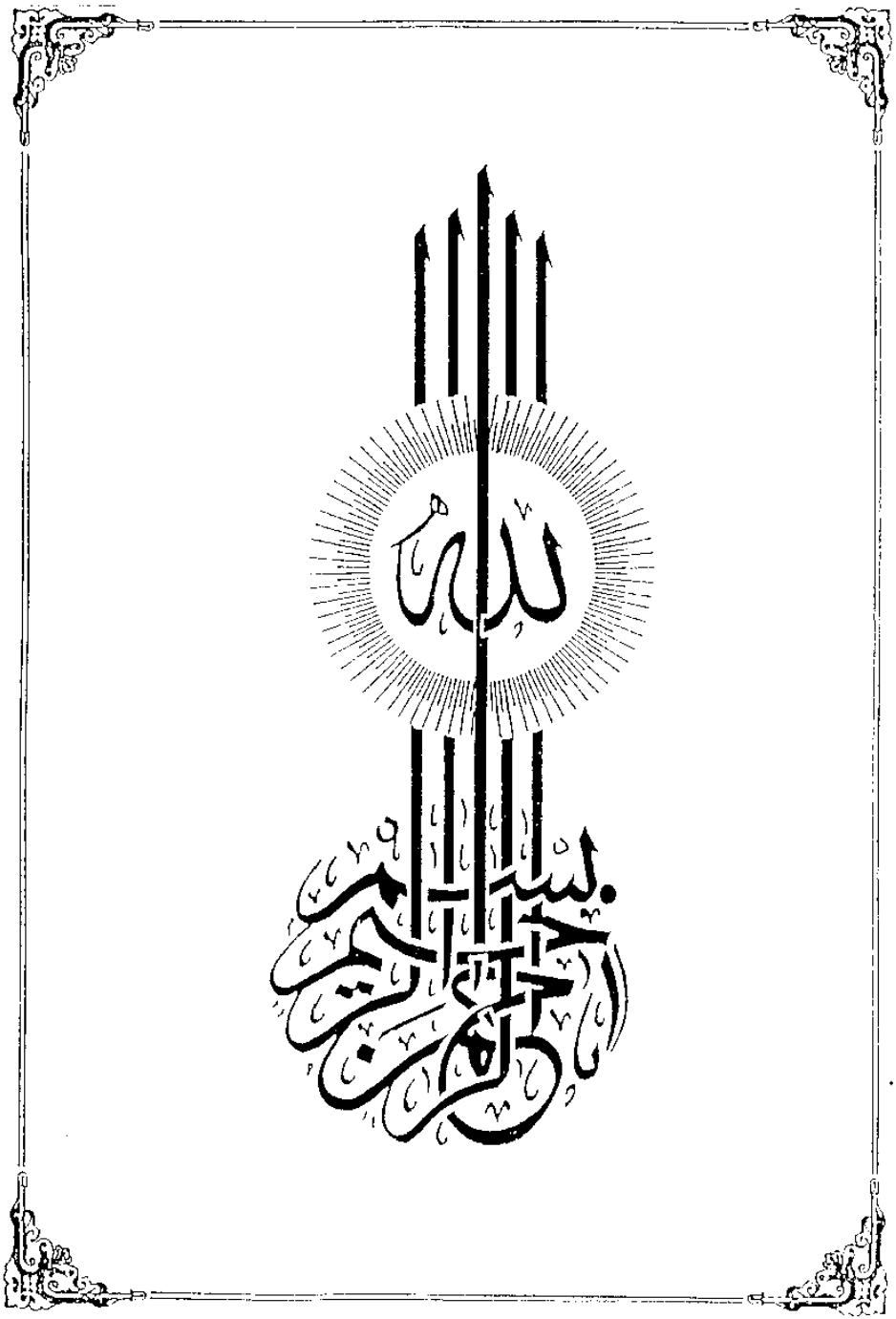

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List of Abbreviations

BFU-E	Burst forming unit- erythroid
bp	Base pair
cAMP	Cyclic adenosine monophosphate
CAPD	Chronic ambulatory peritoneal dialysis
cDNA	Complementary deoxyribonucleic acid
CsA	Cyclosporine
CFU-E	Colony forming unit -erythroid
CFU-GM	Granulocytic macrophage colony forming unit
CFU-MK	Megakaryocytic colony forming unit
CFU-S	Colony forming unit- spleen
CoCl	Cobalt chloride
EPO	Erythropoietin
FPG	Fluorochrome- photolysis-Giemsa
FSH	Follicle stimulating hormone
5-FU	5 fluorouracil
FVA	Friend virus that produces anemia
GVHD	Graft versus host disease
hG-CSF	Human granulocyte colony stimulating factor
hGM-CSF	Human granulocyte macrophage colony stimulating factor
HPLC	High pressure liquid chromatography
IGF-I	Insulin like growth factor
IL	Interleukin
IRMA	Immunoradiometric assay
I-rEPO	Radioactive labelled erythropoietin
Kb	Kilobase

LH	Leutinizing hormone
MDS	Myelodysplastic syndrome
MnCl	Manganese chloride
mRNA	Messenger ribonucleic acid
NiCl	Nickel chloride
PGE	Prostaglandin E
PRCA	Pure red cell aplasia
RA	Rheumatoid arthritis
r-HuEPO	Recombinant human erythropoietin
r-Hu GCSF	Recombinant human granulocytic colony stimulating factor
r-Hu GM-CSF	Recombinant human granulocytic macrophage colony stimulating factor
RIA	Radioimmunoassay
SCD	Sickle cell disease
SV	Simian virus
TCA	Trichloroacetic acid
TFR	Transferrin receptor
TNF	Tumor necrosis factor
TSH	Thyroid stimulating hormone

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AIM OF THE WORK

The aim of the work is to review the mode of synthesis, genetics, chemistry, physiology, regulation and clinical applications of erythropoietin.

The use of recombinant human erythropoietin in the therapy of different types of anemia will also be reviewed.

I-INTRODUCTION

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Normal erythropoiesis is regulated and maintained by a glycoprotein hormone, erythropoietin (EPO) which is synthesized mainly in the kidneys in response to anemia and hypoxia.

Renal synthesis of erythropoietin is regulated by a negative feedback system . Decrease in the concentration of hemoglobin in the blood leads to reduction in the tissue oxygen tension within the kidney. Tissue oxygen tension depends on the relative rates of oxygen supply and demand. Oxygen supply is a complex function of interacting, but semi-independent variables, including blood flow, blood hemoglobin concentration, hemoglobin oxygen saturation and hemoglobin oxygen affinity. Each of these functions may be altered to compensate for a deficiency in one of the others. For example, in severe anemia cardiac output and respiratory rate may increase, and hemoglobin oxygen affinity may be reduced. Conversly, in respiratory insufficiency, secondary polycythemia occurs.

Despite the influence of cardiovascular and respiratory adjustments, tissue oxygen tension decreases roughly in proportion to the degree of anemia. The decrease in the tissue oxygen tension (tissue hypoxia) is sensed by the kidney's oxygen sensor. The kidney responds by increasing erythropoietin.

Red cell progenitors in the bone marrow possess receptors for EPO and are stimulated to proliferate and differentiate.This leads to an increase in the red cell mass (The erythron) and oxygen carrying capacity. The improved tissue