

Title (en)

ERYTHROCYTES AND THROMBO-ERYTHROCYTES AS TARGET SPECIFIC AGENTS.

Title (de)

ERYTHROZYTEN UND THROMBOERYTHROZYTEN ALS ZIELSPEZIFISCHE AGENZIEN.

Title (fr)

ERYTHROCYTES ET THROMBO-ERYTHROCYTES UTILISES COMME AGENTS A SPECIFICITE DE CIBLE.

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Application

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Abstract (en)

[origin: WO9208804A1] The present invention provides new compounds and methods for promoting platelet aggregation, and controlling bleeding. The present invention is based on the surprising discovery that erythrocytes conjugated to certain peptides and polypeptides containing an R-G-D (Arg-Gly-Asp) sequence (collectively termed herein "RGD peptides") according to the invention, selectively bind to activated platelets but not to unactivated platelets. In recognition of the dual nature of the derivatized erythrocytes, they are termed herein "thrombo-erythrocytes". The thrombo-erythrocytes have no significant change in their rheological properties. In a preferred aspect, the thrombo-erythrocytes have the majority of RGD peptide cross-linked specifically to glycoprotein A and glycoprotein B on the surface of the erythrocyte. In the thrombo-erythrocytes of the invention, preferably, the N-terminal Arg of the R-G-D sequence should be spaced within 9-50 Angstroms, more preferably 10-40 Angstroms, and most preferably 11-25 Angstroms, from the erythrocyte protein to which the RGD peptide is conjugated. The invention is further directed to erythrocytes modified by replacement of their intracellular contents with a composition comprising a label or agent. Such modified erythrocytes are termed herein "carrier erythrocytes". The carrier erythrocytes have use in delivery of such labels or biologically active agents to specific tissues by conjugation to a targeting agent.

Abstract (fr)

Procédés et composés nouveaux favorisant l'aggrégation plaquettaire et permettant de contrôler le saignement. Cette invention se fonde sur la découverte surprenante que des érythrocytes conjugués à certains peptides et polypeptides renfermant une séquence R-G-D (Arg-Gly-Asp) (décrite ici sous le nom collectif de "peptides RGD") se fixent de manière sélective sur des plaquettes activées et ne se fixent pas sur des plaquettes non activées. Etant donné la double nature des érythrocytes dérivés, on leur donne le nom de thrombo-érythrocytes. Les thrombo-érythrocytes ne subissent pas de modification significative au niveau de leurs propriétés rhéologiques. Dans une version préférée, les thrombo-érythrocytes ont la majorité du peptide RGD qui est réticulé de manière spécifique à de la glycoprotéine A et à de la glycoprotéine B à la surface de l'érythrocyte. Dans les thrombo-érythrocytes de cette invention, l'Arg à terminaison H de la séquence R-G-D doit être de préférence espacé de 9 à 50 Angstroms, préférablement de 10 à 40 Angstroms et idéalement de 11 à 25 Angstroms, de la protéine d'érythrocyte.

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