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ADENOSINE A2A RECEPTOR AS A INNOVATIVE TARGET TO DESIGN DRUGS FOR DIABETIC ULCERS: FROM PRECLINICAL TO CLINICAL EVALUATION


Diabetic foot ulcers are a leading cause of hospitalization. A reduced formation of new vessels and capillaries is responsible for the poor wound healing observed in diabetes. Adenosine A2A receptor plays a central role in modulating angiogenesis. PDRN (polydeoxyribonucleotide) is a DNA derived drug that engages adenosine A2A receptors. In experimental studies PDRN improved the skin repair process and enhanced wound-breaking strength in diabetic animals. This effect was supported by a marked increase in the expression of Vascular Endothelial Growth Factor (VEGF), a master regulator of angiogenesis that is impaired in diabetes-related wound disorders. The healing-promoting effect was abrogated by adenosine A2A receptor antagonist DMPX. PDRN beneficial effects were confirmed in a clinical trial. Diabetic patient with Wagner grade 1 or 2 ulcers were randomly assigned

to receive placebo (n=106) or PDRN (n=110) for 8 weeks. The drug was injected daily by intramuscular route (5.625 mg in a 3 ml, vial) for 5 day/week and by perilesional route (5.625 mg, in a 3 ml vial) 2 day/week for 8 weeks. The treated group nearly doubled the rate of complete healing of difficult-to-heal diabetic foot ulcers compared to placebo as early as 8 weeks after start of treatment. This study is one of the largest trial ever carried out in diabetic patients with poor diabetic skin repair that points out a dramatic efficacy of PDRN in improving hard-to-heal chronic diabetic foot ulcers and confirms the role of adenosine A2A receptor in diabetes related waound healing disorders.

Biography

Francesco Squadrito has completed his Graduation from University of Messina as Medical Doctor, with the specialties including Clinical Pharmacology and Internal Medicine. Presently, he is full Professor of Pharmacology and Head of the Therapeutic Drug Monitoring Unit at the University of Messina. His research interests are: diabetes related wound healing disorders and metabolic and cardiovascular pharmacology.

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