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Popular Article

Prostaglandin E_2: Its function in reproduction, tissue repair, and regeneration

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Abstract

Prostaglandin E2 is a pro-inflammatory agent and it has various functions in animal reproduction and tissue repair and regeneration. It is an intermediate product of the prostaglandin 2α synthesis pathway. Here we are focusing on the synthesis of prostaglandin E2 from arachidonic acid present in the cell wall.

Introduction

Prostaglandin E_2 (PGE_2) can be produced by nearly all cell types of the body, such as epithelia, fibroblasts, and especially infiltrating inflammatory cells. PGE_2 is synthesized by terminal PGE_2 synthase. Arachidonic acid liberated from membrane phospholipids by several phospholipases, is metabolized by the sequential action of cyclooxygenases (COX) and prostaglandin or thromboxane synthases to produce the diverse classes of prostanoids. These agents are a group of bioactive lipids including prostaglandins (PGs) and thromboxanes (TXs) that play a very important role in many physiological and pathological processes, including cancer, inflammation, angiogenesis, cardiovascular diseases etc. COX enzymes catalyze the formation of an unstable endoperoxide intermediate PGH_2, which in turn can be metabolized by cell-specific isomerases and synthases to a range of eicosanoids with potent and diverse biological effects, as PGD_2, PGE_2, PGF2a, PGI_2, and TXA_2(M. A. In˜iguez et al. 2008). Cytosolic prostaglandin E synthases (cPGES) is a 23 kDa glutathione requiring enzyme coupled with COX-1(Y. Nakatani *et al.*, 2007) and microsomal prostaglandin E synthases1/2 (mPGES1/2) are responsible for the production of PGE_2 from PGH_2. mPGES-1 is mainly coupled with COX-2 to increase the production of PGE_2. Inducible COX-2 is a rate-limiting enzyme for the synthesis of PGE_2. Especially under the stimulant PGE_2 exerts its diverse and complex biologic effects by binding to different downstream prostaglandin E receptors EP1, EP2, EP3, and EP4 that are located on the cell membrane or organelle membrane (Cheng et al., 2021).

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Role of PGE_2 in reproduction

PGE_2 mediates the sex-steroid effect and increased vascular permeability and angiogenesis during implantation and decidualization. PGE2 is only proteinoid involved in decidualization. In the cervix, PGE2 via EP2 and EP4 has been reported to stimulate hyaluronan synthesis in the remodelling of cervical ECM. Various functions of PGE2 are listed in table 1.

Role of PGE_2 in tissue repair and regeneration

PGE_2 displays great promise for the therapy of excisional skin wounds as it participates in different pathological repair processes with its function of anti-inflammatory, promoting angiogenesis, especially preventing scar formation. PGE_2 not only accelerates the healing rate but also remodels the skin structure in injured sites with new hair follicles and sebaceous glands. In the heart with acute myocardial infarction, the production of PGE2 increases significantly in fibroblasts, myocardial cells, and vascular endothelial cells. An accumulating body of evidence indicates that both exogenous and endogenous PGE2 could exert cardiac protection function against ischemia-reperfusion injury. Furthermore, PGE_2 can expedite the repair of liver ischemia-reperfusion injury by reducing liver inflammation, fibrosis and necrosis. Expression of PGE2 may play direct or indirect roles in the immune enhancement of the damaged kidney. PGE2 also exerts anti-fibrotic function in acute renal injury models. In the face of intestinal injury, high local PGE2 levels can induce differentiation of intestinal epithelial stem cells to wound-associated epithelial (WAE) cells instead of enterocytes through EP4 and then the WAE cells migrate to cover and seal the wound bed to re-establish the epithelial barrier (Cheng *et al.*, 2021).

Table 1 - Summary of various functions of PGE2 in reproduction and tissue regeneration

Sr no.	Function		References
1	In reproduction	Role of PGs in Increased Vascular Permeability and Angiogenesis at the Implantation Site	
		Role of PGs in Decidualization	
		Role of PGs in Extracellular Matrix Remodeling	

		Role of PGs in Leukocyte Infiltration	
		Role of PGs in Embryo Transport	
		Role of PGs in Embryo Transport	
		Role of PGs in Blastocyst Growth and Development	
		Role of PGs in Trophoblast Invasion	Salleh *et al.*, 2014
2	In tissue repair and regeneration	myocardial injury and repair	
		hepatic injury and repair	
		renal I/R injury	
		intestinal injury	
		cutaneous wound healing	Cheng *et al.*, 2021

Conclusion

PGE_2 is the most common and biologically active of mammalian prostaglandins. PGE_2 has several medical uses such as inducing parturition, preventing postpartum bleeding, and keeping the ductus arteriosus closed in babies with congenital heart defects.

References

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