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Review

Platelets – an important element of the immune system

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Abstract

Platelets are anucleate cells derived from the megakaryocyte series, and have long been considered only as cells responsible for coagulation and the fibrinolysis process. However, recently more data shows that they are also effector cells in the inflammatory response and important elements of the immunological response. Platelets store and release many biologically active substances, including growth factors, cytokines and chemokines (tab. 1), which actively affect i.a. elements of the immune system, and thus become regulators of immunity and mediators of inflammatory response. Their impact on the immune system cells is also associated with the induction of leucocytes and progenitor cells to the site of pathogen permeation or vascular injury inflow, as well as endothelial cells. Interacting with neutrophils, monocytes and lymphocytes, they not only activate them, but also form platelet-leukocyte aggregates that immobilise pathogens and prevent their spreading. Furthermore, platelets are capable of absorbing pathogens, affecting anti-infection immunity of the system. It is also assumed that the presence of receptors on their surface, such as Toll-like receptors (TLRs), affects their initiation and activity of the immunological response.

Key words: platelets, substances of platelets, receptors of platelets, immune system

Characteristics of platelets

Platelets are anucleate cells derived from the megakaryocyte series, characterised by high morphological variation. Under resting conditions platelets are oval, without cell processes and surrounded with shapeless glycocalyx which prevents their sticking and adhesion e.g. to the endothelium (Stosik and Deptuła 1998, Smorąg and Baj 2008). Their membrane is connected to an intercellular open canalicular system (OCS) which is necessary for their granule content exocytosis which takes part not only in coagulation and homeostasis, but also in inflammation and also activates the immune system (Elzey et al. 2003, Weyrich and Zimmernan 2004, Nurden 2011, Semple et al. 2011, Vieira-de-Abreu et al. 2012). The function of platelets during the immunological response is strictly connected with activation of their surface receptors, including the aforementioned TLR markers and the Fc receptor which recognises immunoglobulins G, E and A as well as selectin P and receptor CD40 (Bocler and Watała 2000,

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Elzey et al. 2003, Blair et al. 2009, Elzey et al. 2011, Semple et al. 2011, Huang et al. 2011, Vieira-de-Abreu et al. 2012). The most important receptors of platelets, in relation to immunological response, are TLRs, which play a major role in the activation of immune system cells, determining the non-specific response, including elements of natural immunity and, indirectly, also the specific response, including acquired (adaptive) immunity components (Blair et al. 2009, Semple et al. 2011, Vieira-de-Abreu et al. 2012). The receptors recognize exogenous and endogenous ligands and bind many various agonists and antagonists, such as antigens of many bacteria, viruses and auto-antigens of vertebrates and invertebrates (Blair et al. 2009, Semple et al. 2011, Vieira-de-Abreu et al. 2012). The occurrence of TLRs on the surface of platelets is evidence of the fact that the cells evolve not only as hemostatic cells, but also as immune system cells, including cells recognising antigens, such as bacterial lipopolysaccharide (LPS). It was evidenced that there are platelets with TLR 1,2,4,5,6 and 9 receptors in humans (Blair at al. 2009, Semple and Freedman 2010, Semple et al. 2011, Nurden 2011, Vieira-de-Abreu et al. 2012). Among them, the role of TLR 4 and 2 was very well recognised and described, as they are also present in mice platelets (Blair at al. 2009, Nurden 2011, Vieira-de-Abreu et al. 2012). *In vitro* studies revealed that, in response to LPS, TLR 4 affects the release of TNFα and induces an interaction between the activated platelets and PMN cells (Vieira-de-Abreu et al. 2012). Furthermore, it was evidenced that TLR4 induces activation of platelets manifested by increasing their adhesion to PMN cell capacity as a result of LPS action. This leads to robust neutrophil activation and formation of neutrophil extracellular traps (NETs) which also prevents bacterial spreading and is very important in severe sepsis (Clark et al. 2007, Pijanowski et al. 2011, Vieira-de-Abreu et al. 2012). Also, *in vivo* studies revealed that the expression of TLR 4 and TLR2 on platelets is changed in patients suffering from diseases related to inflammation of the organism, which evidences their role in immunity (Vieira-de-Abreu et al. 2012). This role is also confirmed by TLR9, present on the platelets, which recognizes bacterial DNA as well as other pathogen ligands, and its expression is increased after activation of platelets with thrombin (Vieira-de-Abreu et al. 2012). The presence of TLR 1, 5 and 6 on the platelets was only evidenced on the level of their expression, yet their role in the activation of platelets is still unknown (Vieira-de-Abreu et al. 2012). Another group of platelet receptors are Fc markers and related to them receptors, including FcγRIIA, Glycoprotein VI (GPVI) and C-type lectin receptor (CLEC-2) (Vieira-de-Abreu et al. 2012), activation of which occurs by phosphorylation of immunoreceptor tyrosine-based activation motifs (ITAM), present in the cytoplasmic part of these receptors, or by binding to subunit FcRγ (Boncler and Watała 2000, Vieira-de-Abreu et al. 2012), as well as receptor CD40 (Elzey et al. 2003, Blumberg et al. 2009, Elzey et al. 2011, Semple at al. 2011, Vieira-de-Abreu et al. 2012). It was evidenced that the presence of receptor FcγRIIA on the platelets depends on the individual features and for its proper expression it is requires one of receptors for collagen – glycoprotein VI (GPVI), and the level of expression of these collagen receptors depends on the platelet activation state (Bocler and Watała 2000). Receptor FcγRIIA is present on human platelets beginning from megakaryocyte maturation stadium (Huang et al. 2011, Vieira-de-Abreu et al. 2012). In humans, it constitutes, together with adhesive protein $\alpha_{IIb}\beta_3$, the main element of the mechanism recognising infection with *Staphylococcus aureus,* which includes binding of IgG class antibodies directed against the bacterium by receptor FcγRIIA and parallel binding of fibrinogen by platelet integrin $\alpha_{IIb}\beta_3$, which leads to platelet activation (Huang et al. 2011, Vieira-de-Abreu et al. 2012). The aforementioned receptors, GPVI and CLEC-2, also contribute to activation of platelet integrin $\alpha_{IIb}\beta_3$ and the release of granules present in the platelets (Vieira-de-Abreu et al. 2012). A major role in platelet activation is also played by selectin P-glycoprotein – one of the adhesive molecules from the selectin group, present on the platelet surface, which determine their participation in the inflammatory process. It was evidenced that platelets increase the production of superoxide anion radical, by binding via selectin P to receptors on neutrophils or monocytes; furthermore, they stimulate, together with platelet-activating factor (PAF), and regulate upon activation normal T cell secreted (RANTES) monocytes to synthesise IL-8, monocyte chemotactic protein-1 (MCP-1), macrophage inflammatory protein 1 alpha (MIP1-α) and tumor necrosis factor alpha (TNF α) (Weyrich et al. 2003, Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012). It was also described that selectin P enhances interaction among platelets and leucocytes as well as endothelial cells (Ważna 2006, Nurden 2011, Vieira-de-Abreu et al. 2012). CD40 receptor is another important and specific receptor of the aforementioned platelets participating in the immunological response, which recognizes molecule CD40L (CD154) (Elzey et al. 2003, Blumberg et al. 2009, Elzey et al. 2011, Semple at al. 2011, Vieira-de-Abreu et al. 2012), the role of which is related to promotion of leucocyte inflow to the inflammation site, interaction between lymphocytes and APC cells, enhancement of cytolytic activity of lym-

Table 1. Biologically active substances of platelets.

Substances		Local within platelet	Reported immune target cells
PF4		α-granules	PMNs, monocytes
RANTES		α-granules	Eosinophils, monocytes, basophils, NK cells, T lymphocytes, DCs
β- thromboglobulins	NAP-2	Not known	PMNs, T lymphocytes, monocytes
	ENA-78	α-granules	PMNs, T lymphocytes, monocytes
MIP-1α		α-granules	Monocytes, DCs, NK cells, basophils, eosinophils, T lymphocytes
CD40L		α-granules and plasma membrane	Leukocytes, endothelial cells, APCs, T and B lymphocytes
IL-1 (α i β)		Not known	Endothelial cells, PMNs, monocytes, T lymphocytes, DCs
PDGF		α-granules	Monocytes, eosinophils, platelets
TGF-β		α-granules	T lymphocytes (Treg and Th17), NK cells, B lymphocytes, PMNs, monocytes
PAF		Plasma membrane	Platelets, PMNs, monocytes
TXA_2		Plasma membrane	Platelets, T lymphocytes
PMP		α-granules	No data

Description: PF4 – platelet factor 4, RANTES- regulated upon activation normal T cell secreted, NAP-2 – neutrophil activating protein 2, ENA-78 – epithelial neutrophil-activating protein 78, MIP-1α- macrophage inflammatory protein 1 α, PDGF – platelet – derived growth factor, TGF-β – transforming growth factor-β, PAF – platelet-activating factor, TXA_2 – tromboksan A_2, PMP – platelet microbicidal proteins

phocytes CTL (CD8+) as well as differentiation of B lymphocytes and switching of immunoglobulin classes.

Biologically active substances of platelets

For a long time it was believed that platelets are incapable of secreting any substances, yet it has turned out that they contain large volumes of pre-mRNA, which they "receive" during formation from megakaryocytes in the bone marrow, and have proteins necessary for post-transcription processing and translation (Weyrich and Zimmerman 2004, Nurden 2011, Vieira-de-Abreu et al. 2012). This makes them capable of synthesising biologically active molecules and their storage in three types of intracellular granules, namely α-granuless, dense granules and lysosomes (Smorąg and Baj 2008, Nurden 2011, Semple et al. 2011). The platelet compounds released or moved to the surface during activation (Table 1) affect the cells and elements forming the immune system (Boehlen and Clemenson 2001, Semple and Freedman 2010, Vieira-de-Abreu et al. 2012).

Platelet factor 4 (PF4) belongs to the CXC chemokine family and is released mainly by activated platelets, but also by T cells. Depending on the target cells, PF4 has pro- and anti-inflammatory effects. *In vitro* studies revealed that it affects the chemotaxis of neutrophils and monocytes and their adhesion to the endothelium and also facilitates migration of such cells through the vessel. Furthermore, PF4 promotes survival of monocytes and their differentiation into macrophages (Stosik and Deptuła 1998, Boehlen and Clemenson 2001, Weyrich and Zimmerman 2004, Vieira-de-Abreu et al. 2012).

RANTES belongs to the subclass of CC chemokines, and is synthesized mainly by T cells, but also by activated platelets (Weyrich and Zimmerman 2004, Vieira-de-Abreu et al. 2012). It was first identified as a platelet chemoattractant for eosinophils, which causes their degranulation and, together with P-selectin, mediates the integration of platelets with monocytes (Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012). It is present in platelet α-granules and quickly released in dissolved form, or as a component of released platelet-derived microvesicles (PMVs), which may additionally function as systems mediating attraction of monocytes, basophils, NK cells and T cells (Boehlen and Clemenson 2001, Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012). RANTES is also the main regulator of CD cell activity (Weyrich and Zimmerman 2004) and has the capacity to block viral infections by binding receptors specific for viruses (Boehlen and Clemenson 2001).

β-thromboglobulins belong to the CXC chemokine family and differ in the length of the N-terminal chain (Weyrich and Zimmerman 2004, Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012). Apart from their presence in the platelets, they are secreted by T cells, monocytes and neutrophils, for which the mentioned proteins are a strong chemoattractant. One of the major proteins among β-globulins is neutrophil activating protein 2 (NAP-2), formed as a result of separation of the C-terminal part of β-thromboglobulin (Weyrich and Zimmerman 2004, Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012). NAP-2 affects formation of neutrophil inflow in the inflammation site or clot formation (Boehlen and Clemenson 2001, Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012). β-thromboglobulins also include epithelial neutrophil-activating protein 78 (ENA-78) with a similar construction to NAP-2. The protein is secreted by platelets and the endothelium of blood vessels, and is a strong chemoattractant for neutrophils. It also increases neutrophil adhesion to the endothelium (Boehlen and Clemenson 2001, Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012).

Macrophage inflammatory protein (MIP-1 α) belongs to a subclass of CC chemokines produced by platelets and by T and B cells, Langerhans cells, neutrophils and macrophages. The pro-inflammatory action of MIP-1α is based on a strong chemotactic action on monocytes, dendritic cells, NK cells, basophils and eosinophils (Boehlen and Clemenson 2001, Semple et al. 2011). Its participation was also evidenced in antiviral response, as it affects attraction of T cells to the viral infection site, what was determined during infection with *Coxsackie virus B3* and influenza A virus (Boehlen and Clemenson 2001, Smorąg and Baj 2008, Semple et al. 2011, Vieira-de-Abreu et al. 2012).

CD 40 Ligand (CD40L, CD154) is a cytokine of the supra-family of TNF-like proteins. CD40L is a trans-membrane protein, principally present on CD4+ T cells, mast cells, B cells, NK cells, but also on platelets (Blumberg et al. 2009, Vieira-de-Abreu et al. 2012). The protein is stored and then exposed on the surface of activated platelets which, via CD40L, bind to the CD40 receptor present on endothelial cells, causing overexpression of adhesive molecules such as intercellular adhesion molecule 1 (ICAM- 1) and vascular cell adhesion molecule 1 (VCAM-1), which leads to chemokine CCL2 release and promotion of leucocyte inflow to the inflammation site (Elzey et al. 2003, Blumberg at al. 2009, Semple and Freedman 2010, Semple et al. 2011, Vieira-de-Abreu et al. 2012). Furthermore, platelets are a source of "free" CD40L in plasma, which may have an impact on blood vessel wall cells (including endothelial cells), inducing overexpression of E-selectin and P-selectin on their surface, as well as secretion of IL-6 and tissue factor (TF) (Semple and Freedman 2010). CD40L protein affects maturation of DC cells and inhibits secretion of pro-inflammatory cytokines IL-12 and TNF by those cells, thus increasing expression of anti-inflammatory IL-10 (Elzey et al. 2003, Blumberg et al. 2009, Elzey et al. 2011, Vieira-de-Abreu et al. 2012). The molecule is also responsible for promotion of the interaction between T cells and antigen-presenting cells (APC), which is evidence that these play a major role in the association of innate and adaptive immunity (Elzey et al. 2011, Vieira-de-Abreu et al. 2012). Furthermore, it is suggested that CD40L is capable of transmitting a direct signal inwards T cell, and strengthening the response of CD8+ T cells by enhanced secretion of IFN-γ, by which it increases their cytolytic activity, e.g. in the case of infection with *Listeria monocytogenes* (Blumberg et al. 2009, Elzey et al. 2011, Vieira-de-Abreu et al. 2012). CD40L may also support differentiation of B cells and switching of immunoglobulin classes from IgM/IgD to IgG, which points to its participation in the acquired immunological response (Elzey et al. 2011, Nurden 2011, Semple et al. 2011, Vieira-de-Abreu et al. 2012).

IL-1α and ILβ – are cytokines with a pleiotropic effect, released both during immunological response and during homeostasis by platelets, monocytes, T cells, neutrophils, fibroblasts and endothelial cells (Boehlen and Clemetson 2001, Smorąg and Baj 2008, Boilard et al. 2010, Vieira-de-Abreu et al. 2012). Activated blood cells are capable of releasing such cytokines both in microvesicles, and in dissolved form in plasma (Vieira-de-Abreu et al. 2012). Such interleukins cause expression of adhesive molecules and chemokines in endothelial cells in humans, and enhance the interaction between endothelial cells on the one hand and PMN cells and monocytes on the other, and also stimulate T cells to express pro-inflammatory molecules (Weyrich and Zimmerman 2004, Boilard et al. 2010, Vieira-de-Abreu et al. 2012). In turn, IL-1β released from platelets is the main regulator of DC cell activity (Weyrich and Zimmerman 2004).

Platelet-derived growth factor (PDGF) is the growth factor mainly produced by activated platelets, but also by monocytes, activated macrophages and endothelial cells. PDGF is a strong chemotactic factor for monocytes and fibroblasts; it also stimulates eosinophils to secrete superoxide anion and inhibits platelet aggregation via autocrine mechanisms (Ważna 2006, Vieira-de-Abreu et al. 2012).

Transforming growth factor-β (TGF-β) is a growth factor produced by stimulated platelets, but also by neutrophils and macrophages. It has an anti-inflammatory effect by inhibiting proliferation of T and

B cells, as well as NK cells, and reduces secretion of many pro-inflammatory cytokines by macrophages. Furthermore, it regulates the activity of lymphocytes T_{reg} and Th17 by affecting transcription factor Foxp3 (Semple et al. 2011). Moreover, TGF-β enhances the production of IgA, and at the same time inhibits secretion of IgM and IgG. This factor also has a chemotactic impact on monocytes, neutrophils and lymphocytes (Semple et al. 2011).

Platelet-activating factor (PAF) belongs to immunomodulating lipids and is principally secreted by mast cells, macrophages and monocytes, as well as by platelets, on which it has autocrine effect. It increases platelet activation caused by ADP (adenosine diphosphate) and thrombins, and induces synthesis of IL-β by platelets (Vieira-de-Abreu et al. 2012). Furthermore, it is a stimulating and chemotactic factor for neutrophils, triggering the release of their lysosomal enzymes and active oxygen species (Smorąg and Baj 2008). It also stimulates formation of platelet-neutrophil and platelet-monocyte aggregates in blood – an important element of immune responses to infections, especially those caused by bacteria (Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012).

Thromboxane A_2 (TXA_2) is one of the pro-inflammatory lipids secreted by platelets. It has both autocrine and paracrine effect on platelets, activating them. It also affects activation and proliferation of T cells and supports their cytotoxic effect (Tilley at al. 2001, Vieira-de-Abreu et al. 2012). It was evidenced that TXA_2 secreted by platelets participates in the mechanism destroying *Toxoplasma gondii.*(Yong et al. 1991)

Platelet microbicidal proteins (PMP) are stored in α-granules and released during platelet activation, showing an antibacterial effect as a result of "recognition" of LPS (Krijgsveld et al. 2000, White 2006, Vieira-de-Abreu et al. 2012). These proteins damage the bacterial cell membrane by increasing its permeability and depolarisation, without damage to the bacterial cell wall (White 2006, Smorąg and Baj 2008). They are lethal to e.g. *Bacillus subtilis, E. coli, Staphylococcus aureus* and *Lactococcus lactis* or *Cryptococcus neoformans* (Krijgsveld et al. 2000).

The role of platelets in immunity

Platelets are important in the "formation" of immunity as the first cells occurring at the site of damage, pathogen permeation, as well as at the inflammation site (Weyrich and Zimmerman 2004, Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012). On the surface of platelets, there is increased expression of receptors specific to antagonists and ligands binding platelets with activated endothelial cells or the stroma of vessels uncovered after infection or trauma, which results in their activation (Smorąg and Baj 2008). The process causes a shape change of such cells from smooth and oval to ameboid (Stosik and Daptuła 1998, Semple et al. 2011), and also a change in their function, as they begin to secrete biologically active substances; this leads to the final and irreversible phase of activation, including aggregation. Cytokines released by platelets, including growth factors and chemokines, regulate immunological response by mobilising and directing leucocytes to the site of the inflammation, and affect the activity of other immune system cells outside the circulatory system (Clark et al. 2007, Smorąg and Baj 2008, Blair et al. 2010, Nurden 2011, Semple et al. 2011, Vieira-de-Abreu et al. 2012). The role of platelets in the modulation of immunological responses has also been noted, pointing i.a. to the action of CD40L as a bridge between innate and adaptive immunity (Semple and Freedman 2010, Elzey et al. 2011, Semple et al. 2011, Vieira-de-Abreu et al. 2012), as it was proven that this molecule induces maturation of dendritic cells (DC) – a base for development of adaptive immunity in response to infections (Semple and Freedman 2010, Elzey et al. 2011, Vieira-de-Abreu et al. 2012). It was also observed that platelets activated in response to viral infections can affect CD40L-dependent differentiation of B cells and switching of immunoglobulin classes, as well as the response of active CD8+ T cells by enhancing their cytotoxic properties against viral antigens (Semple and Freedman 2010, Elzey et al. 2011, Semple et al. 2011, Vieira-de-Abreu et al. 2012). It was hypothesized that platelets affect signal transmission to the interior of various immune system cells as it was evidenced that CD40L causes an increase in IgG secretion even when the number of helper T cells with receptor CD4+ is reduced (Elzey et al. 2005). Hence the presumption (Elzey et al. 2005, 2011) that in physiological conditions where the number of B and T cells and their antigen-specific response is weakened, platelets take over the functions of T cells and cause signal transmission to B cells, in the direction of stimulating specific humoral response. During the inflammation, platelets also affect leucocytes, which leads to the formation of aggregates with neutrophils, monocytes and lymphocytes (Semple and Freedman 2010, Vieira-de-Abreu et al. 2012). This is possible owing to P-selectin present on the membrane of the activated platelets, which binds to P-selectin glycoprotein ligand-1 (PSGL-1), present on the surface of leucocytes. Owing to this, the leucocyte CD11b/CD18-receptor (Mac-1) is activated and, together with platelet glycoprotein IIb/IIIa, binds to fibrinogen, causing strengthening of the bond and for-

mation of platelet-leucocyte aggregates (Smorąg and Baj 2008, Semple and Freedman 2010, Vieira-de-Abreu et al. 2012). P-selectin presented on the surface of activated platelets not only allows their binding to leucocytes, but can also affect activation of leucocytes themselves. It was evidenced that P-selectin, as mentioned earlier, apart from the production of superoxide anion radical in neutrophils and monocytes, together with PAF and RANTES, can stimulate monocytes to synthesis of IL-8, MCP-1, MIP1-α and TNF α (Weyrich et al. 2003, Vieira-de-Abreu et al. 2012). Another mechanism by which platelets can impact the activity of immune system cells is their interaction with the triggering receptor expressed on myeloid cells 1 (TREM- 1) present mainly on neutrophils and monocytes (Semple et al. 2011). Haselmayer et al. (2007) proved that ligand for this receptor is largely expressed in human platelets. They also evidenced that interaction between platelets and neutrophils in the presence of LPS increases TREM-1-dependent neutrophil activation, which results in increased production of reactive oxygen species and release of IL-8 (Haselmayer et al. 2007). It was also evidenced (Semple et al. 2011, Vieira-de-Abreu et al. 2012) that neutrophil- platelet complexes carry out phagocytosis, cytotoxicity or cytolysis more actively than single circulating neutrophils (Semple et al. 2011, Vieira-de-Abreu et al. 2012). It was also observed that platelets affect PMN cells causing formation of NETs, mainly in bacterial infections e.g. in severe sepsis (Clark et al. 2007, Semple et al. 2011, Vieira-de-Abreu et al. 2012). *In vitro* studies of this process indicate the major role of platelet TLR4, which is responsible for binding bacterial LPS (Clark et al. 2007). It was also evidenced that interaction of platelets and monocytes induces translocation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), and expression of NF-κB-dependent genes and proteins in monocytes, involved in the regulation of the inflammation, as a result of action of platelet-derived RANTES, IL-1β and PAF, which increase the secretion of e.g. TNFα, IL-8 and MCP-1 in monocytes (Weyrich et al. 1995, Smorąg and Baj 2008, Vieira-de-Abreu et al. 2012). *In vitro* studies indicate that platelets also contribute to acceleration of chemokine synthesis in monocytes, and that they can provide the "signal" which triggers monocyte differentiation into DC cells rather than into settled macrophages (Weyrich et al. 1995, Vieira-de-Abreu et al. 2012). The least data refer to the interaction between platelets and lymphocytes; it is only known that activated platelets secrete substances acting as chemoattractants and have an activating effect on helper T cells (Th), cytotoxic T cells (Tc) and NK cells, as well as B cells (Li 2008). As mentioned earlier, T cells can contribute to platelet secretion of RANTES chemokine, as a result of a mechanism dependent on CD40L-CD40, which increases the inflow of lymphocytes to the inflammation site. Also, platelets facilitate lymphocyte aggregation in lymph nodes, which contributes to the formation of immunological memory (Vieira-de-Abreu et al. 2012). Moreover, platelets activate Tc cells in response to viral infections, e.g. during hepatitis B virus infection, as they affect the accumulation of such lymphocytes in the liver (Semple et al. 2011). It was evidenced that the role of platelets in anti-infection immunity of the system is related to the fact that they are capable of destroying pathogens both indirectly – by involving other cells of the immune system, as well as directly, by secretion of substances destroying and damaging bacteria, such as PMP or reactive forms of oxygen (Semple and Freedman 2010, Nurden 2011, Vieira-de-Abreu et al. 2012). Furthermore, their effect on pathogens is not only limited to the release of active substances from granules, but they are also capable of absorbing small extraneous molecules via an open canalicular system, without activation or changing shape (Stosik and Deptuła 1998). They detect bacteria in the circulatory system and surround them by adhesion, and hence it is assumed that their activity can be helpful in "clearing" microorganisms from the blood, which prevents their spreading across the system, even despite the fact that they are not professional phagocytes (Stosik and Deptuła 1998, Smorąg and Baj 2008).

Conclusion

Previous studies on platelets, which once were regarded only as megakaryocyte cytoplasm fragments, indicate that they constitute an important element of the immune system, including natural immunity, and also of acquired immunity by their interaction with B cells. This is due to their unique properties, such as the capacity of expressing receptors and secretion of pro- and anti-inflammatory substances, as well as their capacity of interaction with granulocytes, monocytes and lymphocytes. The data indicate the important role in platelet function as an essential element in maintaining the antigen integrity of the entire organism.

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