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Inflammatory responses of primary human dendritic cells towards polydimethylsiloxane and polytetrafluoroethylene

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Abstract

Although frequently used as implants materials, both polydimethylsiloxane (PDMS) and polytetrafluoroethylene (PTFE) are often associated with adverse effects including foreign body responses. Dendritic cells (DC) are crucial for the initiation of immune reactions and could also play a role in foreign body associated inflammations. Therefore, the interaction of DC with PDMS and PTFE was investigated regarding their capacity to induce undesired cell activation.

Medical grade PDMS and PTFE films were embedded into polystyrene PS inserts via injection molding to prevent the DC from migrating below the substrate and thereby, interacting not only with the test sample but also with the culture vessel material. The viability, the expression of co-stimulatory molecules, and the cytokine/chemokine profiles were determined after 24 hours incubation of the DC with PDMS or PTFE. Blank PS inserts and tissue culture polystyrene (TCP) served as reference materials. The viability of DC was not substantially influenced after incubation with PDMS and PTFE. However, both polymers induced DC activation indicated by the upregulation of co-stimulatory molecules. The release profiles of 14 soluble inflammatory mediators showed substantial differences between PDMS, PTFE, PS and TCP. This study showed the potential of PTFE and PDMS to activate primary human dendritic cells, which could be an explanation for the often observed inflammatory events associated with the implantation of these polymers.

Keywords: biomaterials; dendritic cells; polydimethylsiloxane; polytetrafluoroethylene; cell culture devices

Introduction

Polydimethylsiloxane (PDMS) and polytetrafluoroethylene (PTFE) are polymers frequently used in clinical applications as implant materials. For example, PDMS is widely used in catheters, shunts, implants for plastic surgery or artificial larynx, while PTFE is used as biomaterial for prosthetic bypass grafts or hernia meshes [1-3]. Due to their relative inertness both polymers show an acceptable biocompatibility. Although systemic complications associated with PDMS implants, are relatively rare, it is assumed that local immunological effects directed against an implant occur in up to 50% of patients [4]. A strong association with inflammatory cells was also observed in PTFE hernia meshes [5]. Such immunological effects can initiate a foreign body reaction (FBR), which is directed against the implanted biomaterial and can occur immediately after implantation or several years later. As consequence, the implant may lose its functionality requiring its replacement, which is associated with additional discomfort and suffering for the patient. Macrophages are considered as key driver of the FBR, since they are often found to adhere at the implant interphase subsequently forming foreign body giant cells, which facilitate the acute inflammatory reaction [6]. However, the FBR can also have chronic characteristics implying that not only cells of the innate immune system such as macrophages, but also cells of the adaptive immune system including T and B cells can be involved in this process [7]. In fact, these cells were found randomly distributed in the fibrotic capsule formed around the implant area [16]. More specifically, pro-inflammatory T_h17 cells and suppressive regulatory T cells (Treg), whose ratio was inversely correlated with the clinical degree of capsular fibrosis, were found on silicone implants, indicating that the balance between regulatory and effector T cells could determine the progression of the FBR [8]. Dendritic cells (DC) bridge the innate and adaptive immune system and can initiate and modulate T cell responses by antigen presentation and cytokine secretion, respectively. DC can be activated by foreign structures such as microbial products, but also by artificial surfaces including polymeric biomaterials [9]. For example, different polymethacrylates can induce the expression of co-stimulatory molecules as well as the expression of inflammatory cytokines [10]. Furthermore, polystyrene (PS), polycarbonate (PC), poly(ether imide) (PEI), and poly(styrene-*co*-acrylonitrile) (PSAN) were found to induce the secretion of distinct cytokines [11]. These data indicated that the different material properties such as the chemical composition can induce DC responses. In fact, the interaction of murine bone

marrow-derived DC with non-medical grade PDMS and PTFE has already been investigated showing that PTFE induced the upregulation of CD86 and of tumor necrosis factor (TNF)-α, whereas only minor effects were observed when the DC were cultivated on PDMS [12]. The PDMS and PTFE-induced DC activation led to an enhanced T cell proliferation [12]. Therefore, it is rational to ask whether similar effects are induced in primary human DC when cultivated on clinically used PTFE and PDMS, which might explain some of the often observed adverse effects. Since cytokines and chemokines released by DC can determine and modulate the course of the immune response, the secretion profile of 20 inflammatory meditators was additionally analyzed.

For these investigations medical grade PTFE and PDMS films were embedded into PS-based inserts by using the injection molding process. Thereby, it could be ensured that the PTFE and PDMS films were tightly fixed at the bottom of the cell culture vessel avoiding that cells migrate below the substrates and additionally interact with the cell culture vessel. Except for TCP all substrates showed advancing water contact angles (θ_{adv}) in the same range as blank PS 99° ± 5°, PTFE 119° ± 3° and PDMS 104° ± 1°, while TCP had a contact angle of 21° ± 1° as determined at ambient temperature. Comparing the wettability of the four substrates used, only TCP can be considered as hydrophilic since θ_{adv} was below 65° [13]. The blank PS insert surface, PTFE, and PDMS are rather hydrophobic since their contact angles θ_{adv} were above 95°. The roughness levels are in nm range for all substrates ($R_{q,TCP}$ = 10 ± 3 nm, $R_{q,blankPS}$ = 0.3 ± 0.1 nm, $R_{q,PTFE}$ = 62 ± 6 nm, and $R_{q,PDMS}$ = 14 ± 2 nm) with PTFE showing the highest roughness, while PS had the lowest.

Human primary monocyte-derived DC were isolated from buffy coats and differentiated into DC using IL-4 and GM-CSF and incubated for 24 hours on the different substrates. The viability and expression of co-stimulatory molecules by DC was determined by flow cytometry. The cytokine and chemokine secretion pattern were analyzed in DC supernatants by a multiplex suspension assay.

Material and Methods

The study was performed in accordance with the ethical guidelines of the journal *Clinical Hemorheology and Microcirculation* [14].

Processing of the polymeric inserts with embedded PDMS and PTFE films

Polystyrene (PS, Type158K, BASF, Germany) with a number average molecular weight of M_n = 109.000 g·mol^{-1}, was processed into cell culture inserts fitting into a 24-well plate using an injection molding automat (Alrounder 270U, Arburg Corp., Münsingen, Switzerland) equipped with a custom made mold (Dreuco Formenbau GmbH, Berlin, Germany), as previously described [11]. Medical grade PDMS and PTFE films (Bess Medizintechnik GmbH, Berlin, Germany) were cut into circular specimens with a diameter of 11.5 mm, placed in the custom made injection molding mold and processed via injection molding of PS at a temperature of 230 °C and an injection pressure of 90-110 MPa to achieve PDMS and PTFE inserts [15]. Prior to biological experiments all inserts were sterilized with ethylene oxide gas as previously reported [16]. The endotoxin levels of the inserts were determined as previously described [11] and all inserts showed endotoxin levels below 0.06 EU·mL^{-1}, which is well below the limit defined by the U.S. Food and Drug Administration for medical devices [17]. Sterile, pyrogen-free, and corona discharge-treated TCP purchased from TPP (Trasadingen, Switzerland) was used as reference material. The corona treatment process generates highly energetic oxygen ions, which graft onto the polystyrene surface chains resulting in an increased surface hydrophilicity faciliting the cell attachment [18].

Generation of peripheral blood mononuclear cells (PBMC) derived dendritic cells

PBMC were isolated as previously described by density gradient centrifugation using Biocoll^{TM} (Biochrom AG, Berlin, Germany) from buffy coats of healthy human individuals [19]. Monocytes were purified from PBMC by depleting the CD14 negative cells using the monocytes isolation KitII (Miltenyi Biotec, Bergisch-Gladbach, Germany). For all donors the purity of the isolated CD14 positive monocytes was above 95% as determined by flow cytometry. DC were generated by adding 10 µg·mL^{-1} interleukin(IL)-4 (Milteniy Biotec) and 100 µg·mL^{-1} granulocyte macrophage - colony stimulating factor (GM-CSF) (Milteniy Biotec) to the monocytes preparation for six days. The differentiated DC were harvested and 1×10^6 cells were

seeded into the different inserts and TCP for 24 hours with or without 1 $\mu g \cdot mL^{-1}$ lipopolysaccharides (LPS) (LPS from *E.coli* O111:B4, Axxora GmbH, Lörrach, Germany). The successful differentiation of the CD14 positive monocytes into DC was checked by CD14 and CD209 expression and resulted routinely in more than 98% $CD209^{high}$ and $CD14^{low}$ cells.

Flow cytometry analysis for surface molecule expression

After exposure to the PDMS, PTFE, PS control inserts, and TCP the cells were harvested and washed with AutoMacs® washing buffer (Milteniy Biotec). The staining procedure was performed as described previously [19]. Briefly, to avoid unspecific antibody binding to Fc-receptors, FcR-Blocking Reagent (1:100, Milteniy Biotec) was used. DC were discriminated from monocytes by staining with anti-CD14-PE-Vio770 (clone TÜK4, Milteniy Biotec) and anti-CD209-APC (clone DCN47.5, Milteniy Biotec). To determine the activation status of the DC, the following antibodies were used: anti-CD86-FITC (clone FM95, Milteniy Biotec), anti-CD80-PE (clone L307.4, BD Biosciences, San Jose, USA), anti-CD83-FITC (clone HB15e, R&D Systems Inc., Minneapolis, USA), anti-HLA-ABC-PE (clone G46-2.6, BD Biosciences), anti-CD40-FITC (clone 5C3, BD Biosciences, Heidelberg, Germany), and anti-HLA-DR-PE (clone AC122, Milteniy Biotec). Cells were stained for ten minutes on ice. After a final washing step, 1 $\mu g \cdot mL^{-1}$ 4',6-diamidino-2-phenylindole (DAPI) (Roth, Karlsruhe, Germany) was added immediately prior to acquisition to discriminate live from dead cells. Sample acquisition was performed using the MACSQuant® analyser (Milteniy Biotec).

Multiplex cytokine profiling of DC cell culture supernatants

DC culture supernatants were harvested and stored at -20 °C until further usage. The cytokine secretion was quantified in thawed supernatants using multi-plex suspension array systems (Bio-Plex 200®, BioRad, Germany) according to the manufacturer's instructions. All bead assays were purchased from BioRad. The secretion of IL-1ra, IL-1β, IL-6, IL-8, IL-9, IL-10, IL-12, IL-17, eotaxin, granulocyte-colony stimulating factor (G-CSF), granulocyte macrophage-colony stimulating factor (GM-CSF), interferon(IFN)-γ, interferon-gamma induced protein 10 kD (IP-10), chemokine (C-C motif) ligand (CCL) CCL2, CCL3, CCL4, CCL5, platelet-derived growth factor (PDGF)-BB, and tumor necrosis factor(TNF)-α was determined.

Data analysis

Statistical analysis and graphical representation were performed using GraphPad Prism version 6.02 for Windows, (GraphPad Software, La Jolla, California, USA). One-Way Anova followed by the Tukeys multiple comparisons test was used to statistically compare the mean of every experimental group with the mean of every other group. Unless otherwise indicated the mean ± standard deviation is shown with **** for $p<0.0001$; *** for $p<0.001$; ** for $p<0.01$; and * for $p<0.5$.

Hierarchical clustering analysis (HCA) of the cytokine secretion levels was performed with the MeV program (version 4.9.0) using Pearson correlation and average linkage as previously described [20]. Prior to the HCA analysis data were normalized by the MeV software using the following: Value = [(Value) – Mean(Row)]/[Standard deviation(Row)]

Flow cytometry data were analyzed using FlowJo vX10.0.7 software (Tree Star, Ashland, USA).

Results

To investigate the interaction of DC with PTFE and PDMS both polymers have been embedded into PS inserts, which were previously shown to be compatible with DC [11]. The embedding led to a tight fixation of PTFE and PDMS films at the bottom of the PS inserts, thereby avoiding cells to migrate below the test sample and interacting not only with the test sample, but also with the cell culture vessel. For all substrates the endotoxin levels were below the detection limit of the used assay, indicating germ-free manufacturing process. This is mandatory when studying cells expressing toll-like receptor (TLR) 4 including DC, since material-associated endotoxins can substantially bias the cellular readout by activating the TLR pathway [21].

To study the interaction of DC with PDMS and PTFE, the cells were cultivated for 24 hours on the different polymeric substrates and commercially available TCP, which served as reference material.

The morphology of DC cultures can give implications about the activation status of the cells. Non-activated DC appear as individual cells as observed for untreated DC cultivate on TCP (Fig. 1 A). In contrast, the addition of LPS induced aggregation of

DC, which is indicated by the formation of large cell clusters (Fig. 1 E). DC cultivated in the PS insert showed a slight aggregation, which was more pronounced when the DC have been cultivated on PTFE and PDMS embedded into PS inserts (Fig. 1 B, C, D). LPS-activated DC cultivated on PS, PTFE and PDMS showed cluster formation similar to the TCP control and no differences between the polymers could be observed (Fig. 1 E, F, G, and H).

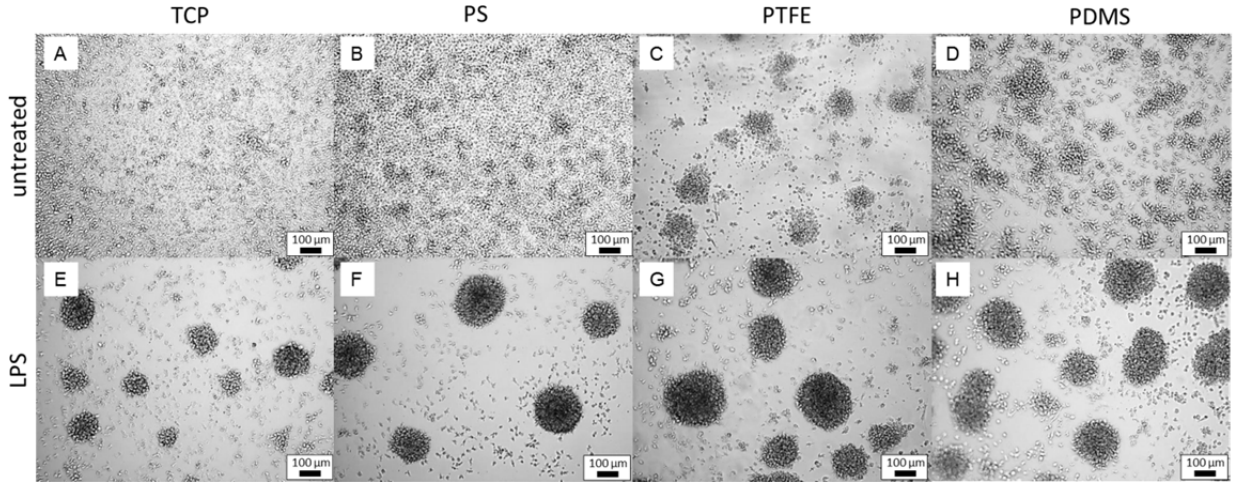

Figure 1: Morphology of DC culture after exposure to the different polymeric substrates. Human PBMC-derived DC were left untreated (A, B, C, D) or were activated with 1 µg·mL^{-1} LPS (E, F, G, H) and cultivated for 24 hours in the different inserts. Light microscopic images are representative for DC cultures of eight individual donors.

Implant-induced cell death could be an accelerator of the inflammatory reaction, since certain molecules released by death cells can orchestrate the inflammatory responses [22]. Therefore, it was analyzed whether PTFE and PDMS can have an impact on the DC survival, which was determined by flow cytometry using DAPI incorporation as dead cell indicator. No significant differences could be observed when the DC survival on TCP was compared to PS, PTFE, and PDMS. Compared to PS and PTFE the amount of live cells was slightly reduced on PDMS (Fig. 2). When DC were activated with LPS, PDMS seems to support the DC survival since the amount of live cells was higher compared to TCP (Fig 2). Conclusively, the data indicate that PDMS has moderate effects on the DC survival for both untreated and LPS-activated DC.

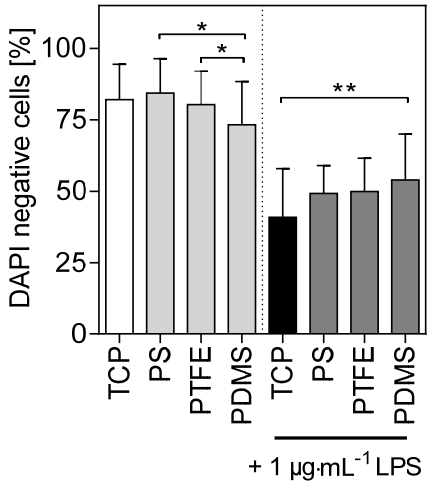

Figure 2: Survival of DC after cultivation on PTFE and PDMS. The DC were cultured for 24 hours on PTFE, PDMS, PS, or on TCP and either left untreated or stimulated with 1 µg·mL^{-1} LPS. The amount of dead cells was determined by flow cytometry according to DAPI incorporation and applying the gating strategy as previously described [19]. Data represent average percentage of eight donors (n=8) analyzed in three independent experiments (mean ± standard deviation (SD)).

Next, it was assessed whether the slightly impaired DC survival on PDMS is a direct cell death-inducing effect or a physiological consequence of a PDMS-mediated cell activation, which was already indicated by the cell culture morphology and would subsequently lead to apoptosis induction [23]. Therefore, the activation status of the DC was determined according to their expression of surface molecules including the co-stimulatory molecules CD40, CD80, and CD86 as well as the activation and maturation-induced factors HLA-DR, CD83, and HLA-ABC. Indeed, it was found that DC cultivated on PDMS showed the highest levels of CD40, CD80 and CD83 expression, while PTFE only induced the expression of CD40 (Fig. 3). The levels of CD86, HLA-DR and HLA-ABC remained unchanged indicating that neither PTFE nor PDMS had an influence on these molecules. Interestingly, the expression of CD40 and CD80 was slightly reduced when LPS-activated DC were cultivated on PS, PTFE, and PDMS (Fig. 3). The expression levels of CD83, CD86, HLA-DR, and HLA-ABC of LPS-activated DC were not substantially altered by PTFE and PDMS and remained comparable to TCP (Fig 3.). In conclusion, the analysis of the surface molecule expression levels confirmed that PDMS is able to activate the DC, which would also explain their increased cell death after cultivation on PDMS.

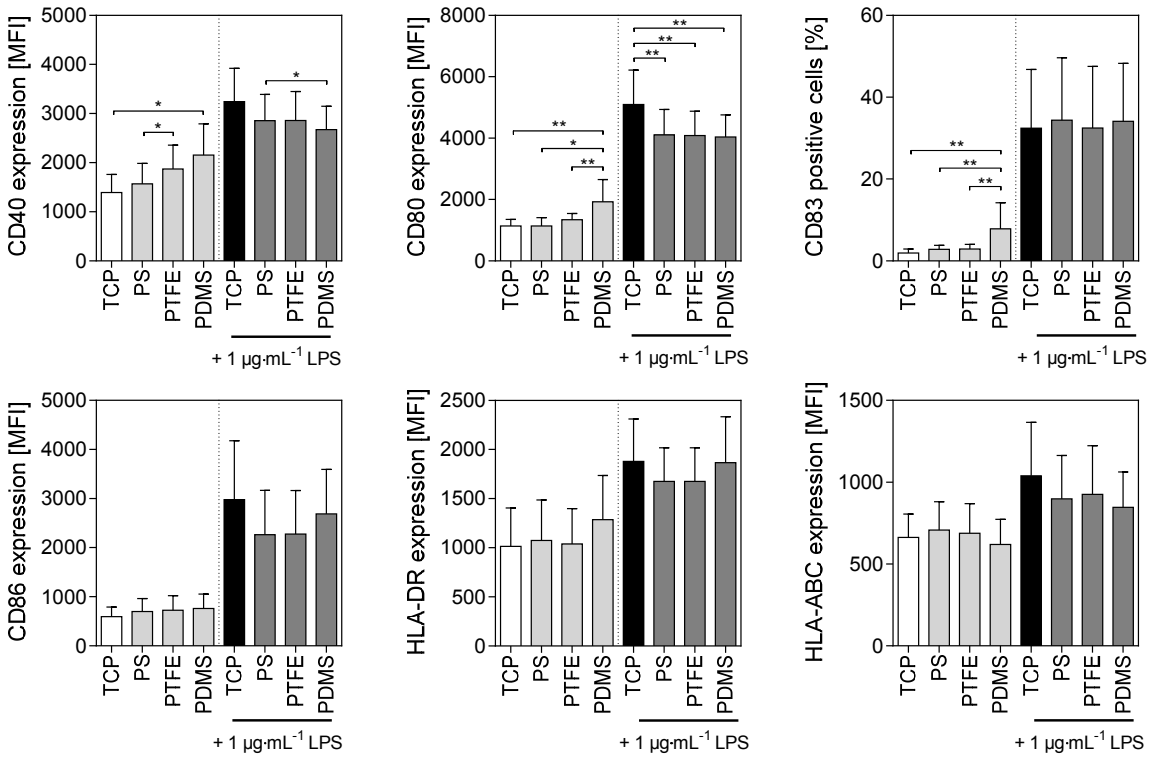

Figure 3: Surface molecule expression levels on DC after exposure to PTFE and PDMS. DC were cultivated for 24 hours on PTFE, PDMS, PS, or on TCP, with or without 1 µg·mL^{-1} LPS. Expression levels of CD40, CD80, CD83, CD86, HLA-DR, and HLA-ABC were analyzed by flow cytometry after doublet exclusion on DAPI negative (live) cells as previously described [16]. The fold induction of the average median fluorescence intensities (MFI) of DC from eight healthy donors analyzed in three independent experiments (n=8) is depicted (mean ± SD).

The release of cytokines and chemokines by activated DC regulates the initiation and the progression of immune responses by primarily acting on T cells. Therefore, it is of importance to determine the cytokine/chemokine profile of DC in order to anticipate the kind of the potential immune reaction. To analyze cytokine/chemokine secretion by DC in response to the different substrates, the cell culture supernatants were collected after 24 hours of incubation and a multiplex analysis for 19 secreted factors was performed. The secretion levels of IL-1β, IL-1ra, IL-9, IL-10, IL-12, eotaxin, and GM-CSF were either out of the detection range or did not show significant differences (data not shown).

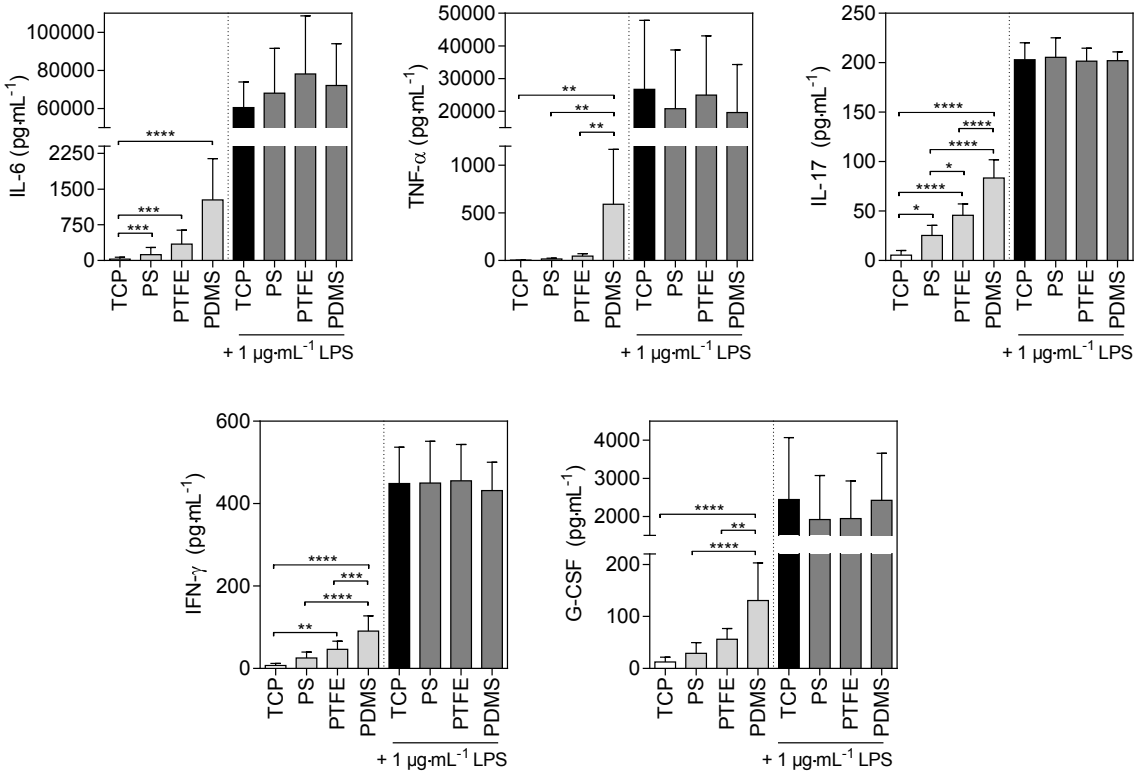

Figure 4: Cytokine expression by DC after cultivation on PTFE and PDMS. DC were cultivated for 24 hours on PTFE, PDMS, PS or in TCP, with or without 1 µg·mL^{-1} LPS. Release of IL-6, TNF-α, IL-17, IFN-γ, and G-CSF was analyzed by a multiplex assay. The average of eight healthy donors analyzed in three independent experiments (n=8) is shown (mean ± SD).

Compared to TCP, PS and PTFE only induced moderate amounts of pro-inflammatory cytokines including IL-6, TNF-α, IL-17, IFN-γ, and G-CSF, while substantially higher level of these cytokines were secreted by DC that have been cultivated on PDMS (Fig. 4). The LPS-induced cytokine secretion was not altered by the different polymers (Fig. 4). Besides cytokines also chemokine can influence the DC-induced immune response by acting on T cells or attracting other immune cells. The secretion of chemokines was analyzed in DC supernatants. As observed for cytokines also chemokines including IL-8, IP-10, CCL3, CCL4, CCL5 and PDGF-BB were strongly induced by PDMS (Fig. 5). PTFE induced substantial amounts of IL-8, IP-10, CCL4, and PDGF-BB, while the PS insert showed cytokine levels similar to the TCP control (Fig. 5). With exception of PDGF-BB no differential chemokine expression could be observed when LPS-activated DC were cultivated on the different polymers. The LPS-induced expression of PDGF-BB was further increased when DC were cultivated on PS, PTFE, and PDMS (Fig. 5).

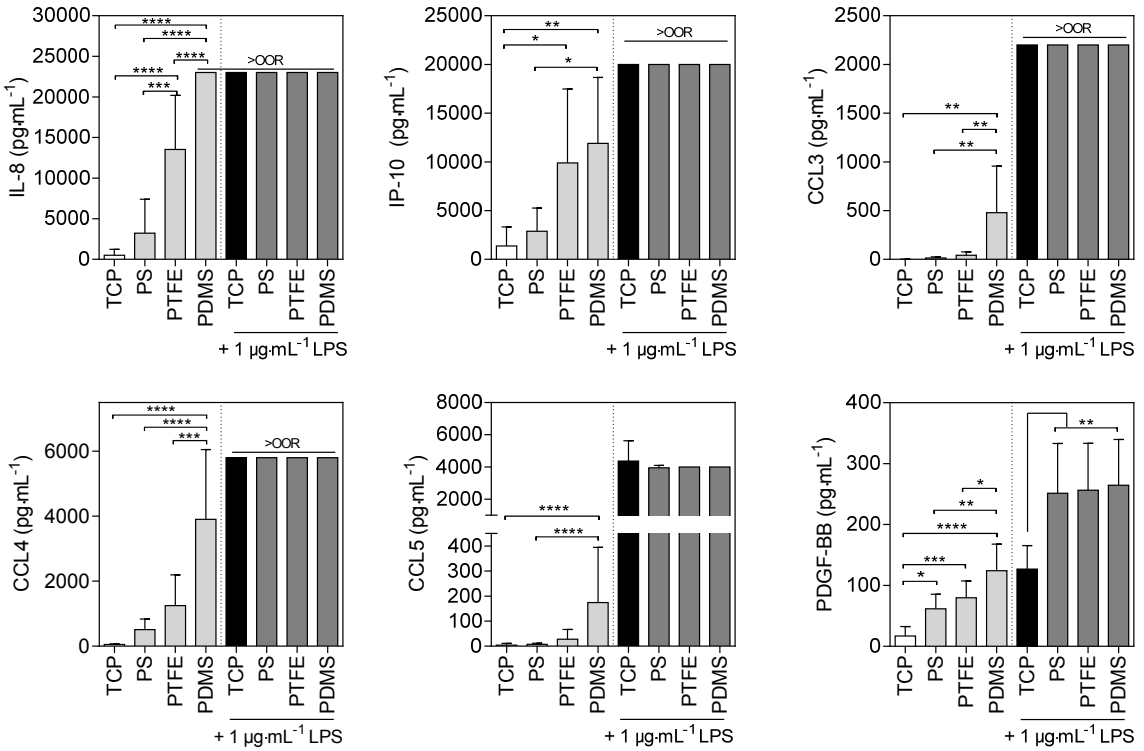

Figure 5: Chemokine secretion by DC after cultivation on PTFE and PDMS. DC were cultivated for 24 hours on PTFE, PDMS, PS, or in TCP, with or without 1 µg·mL^{-1} LPS. Release of IL-8, IP-10, CCL3, CCL4, CCL5, and PDGF-BB was analyzed using the BioPlex® multiplex system. The average of eight healthy donors analyzed in three independent experiments (n=8) is shown (mean ± SD).

In order to identify distinct cytokine/chemokine pattern secreted by DC post cultivation on the different polymeric substrates and to pinpoint possible regulatory relations between the cytokine secretion profiles a hierarchical cluster analysis (HCA) was performed. This analysis can highlight linkages of factors or samples with similar behavior indicated by the distance of the “branches”. As closer the “branches” are as more similar may cytokine/chemokine be regulated potentially involving the same signaling pathway. Additionally, differences among the polymers regarding their capacity to induced cytokine/chemokine production in DC can be visualized with the aim to identify substrates that induce similar or opposite cell response. For the HCA performed here only cytokines/chemokines showing a release above 50 µg·mL^{-1} for at least one donor and one experimental condition were included. The HCA of the cytokine/chemokine secretion by DC cultivated on TCP, PS, PTFE, and PDMS confirms that PDMS is the most potent inducer of cytokine/chemokine release followed by PTFE. While IP-10, CCL2, IL-8, IFN-γ, IL-17, IL-1ra, and PDGF-BB seem to be upregulated in the same fashion by PTFE and PDMS, G-CSF, CCL4, IL-6,

IL-10, CCL5, CCL3 and TNF-α are induced only by PDMS indicating that PDMS activates additional pathways leading to the release of these cytokines (Fig. 6). PS and TCP behave very similar (Fig. 6). Conclusively, the cytokine/chemokine expression data indicate that PTFE and PDMS induce substantial amounts of several inflammatory mediators with distinct expression pattern indicating that both polymers activate or inhibit different signaling pathways.

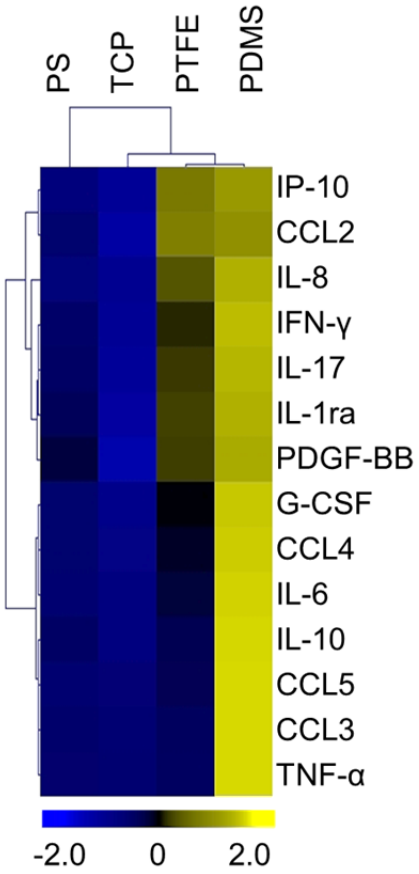

Figure 6: Hierarchical clustering of 14 cytokines expressed by DC. The cytokine amounts detected by a multiplex assay were used for the HCA after normalization was performed. The average expression values of eight individual donors were used for the HCA. Up-regulated factors are shown in yellow and down-regulated factors are displayed in blue.

Discussion

Almost every biomaterial can induce inflammatory reaction after implantation and the underlying mechanism are in most cases poorly understood [24]. It is insufficiently known which signals the biomaterial interphase provides to the cells leading to the initiation of unwanted side effects such as inflammation. Additionally, it is also poorly described, which signaling pathways are activated inducing certain cell responses particularly in immune cell subsets. To analyze material-induced cell responses, the

biomaterial sample is mostly processed into disks, which can be placed into cell culture wells [25]. However, those material samples can often freely move within the cell culture well and may not remain at the bottom of the well requiring fixation of the sample with another material. As consequence the cells of interest can potentially interact with the three different materials; the cell culture vessel material typically tissue culture polystyrene, which is usually corona discharged treated to generate highly energetic oxygen ions resulting in an increased surface hydrophilicity and cell attachment [18]. The second material which is used to fix the sample is mostly a glass or PTFE ring and the third material would be the actual sample. For this reason, the interpretation of observed effects might be challenging. To circumvent this issue an insert system in which the polymeric test sample was tightly fixed at the bottom of the vessel was presented here. Both, adherent and non-adherent cells will sediment on the bottom of the insert and interact with the test sample. As insert material PS was chosen, since it was previously shown that it has negligible effects on DC and it is most comparable to TCP [11].

The survival of immune cells on implant materials could be an important parameter for the physiological consequence. Antigen presenting cells including DC undergo apoptosis soon after activation to limit their capacity to activate T cells and thereby to maintain self-tolerance and prevent autoimmune pathologies [23]. This could explain the slightly decreased survival of DC after cultivation on PDMS. An increased survival rate as observed for DC activated with LPS and cultivated on PDMS may however promote chronic immune reactions. Whether this effect can also be observed for other activation or maturation-inducing factors, such as TNF-α, HMGB1, heat shock proteins, or extracellular matrix fragments, which may appear during the FBR and whose release could be mediated by immune cell or dead cells, need to be elucidated [22].

The expression of co-stimulatory molecules, certain cytokines, and chemokines was significantly increased when DC were cultivated on PDMS. These observations indicated that such DC could initiate, potentiate or modulate a subsequent T cell response. A similar effect was already observed for human macrophages [26]. Compared to macrophages, DC are considered as semi-adherent. Nevertheless, they may also interact with adsorbed proteins in the same fashion as macrophages do. In fact, the proteins layer adsorbed onto the biomaterial surface is a key factor that determines the cellular responses. Protein adsorption depends on the wettability

of the surface. Hydrophobic surfaces generally adsorb higher amounts of proteins and also denature the proteins [27]. Compared to TCP, which has a hydrophilic surface, the contact angle of PS insert, PTFE and PDMS indicates a hydrophobic surface. However, this alone cannot explain the observed DC activation by PDMS, since PS and PTFE show a similar contact angle but did not induce DC activation. Another surface property that can influence the DC behavior is the surface roughness. For example, different roughness levels in the µm range can alter the cytokine/chemokine expression of DC as shown for polymers including PS and poly(ether imide), but also for clinical titanium surfaces treated by sand blasting and acid etching [16,28]. However, all substrates used in this study had roughness levels in nm range, indicating that this surface property is also not responsible for the observed PDMS-mediated DC activation. Though, it is likely that the combination of the different physical and chemical parameters can induce distinct DC responses.

While PTFE induced a moderate DC activation PDMS showed a substantially stronger DC response indicated by the induced expression of co-stimulatory molecules and the enhanced secretion of cytokines and chemokines. By using murine bone marrow-derived DC, it was previously demonstrated that PFTE induced a stronger DC activation than PDMS [12]. However, the data for human DC obtained in this study cannot confirm these findings, indicating that DC responses can be species specific and may also depend on the source of the DC and the used differentiation protocol.

As consequence of the observed PDMS-induced DC activation, the subsequent T cell response could be facilitated. For example, CCL2, which was highly secreted by DC cultivated on PDMS, is a potent attractor for monocytes and T cells, which can induce and facilitate foreign body reaction against implants [9]. Investigations aiming to understand the chemokine inducing mechanisms in immune cells, will be performed in future. The HCA showed that not only the amount of cytokines released by DC cultivated on PDMS was higher compared to all other condition, but also the type of cytokines/chemokines was different. While PTFE induced IP-10, CCL2, IL-8, IFN-γ, IL-17, IL-1ra and PDGF-BB, PDMS additionally induced the secretion of G-CSF, CCL4, IL-6, IL-10, CCL5, CCL3 and TNF-α, implying that PDMS activated other cellular signaling pathways than PTFE. The receptors and signaling pathways involved in the PDMS-mediated DC activation will be investigated in the future for instance by using small molecule inhibitors or siRNA.

Conclusion

The study investigated the interaction of medical grade PDMS and PTFE with DC. The data obtained demonstrated that PDMS is a potent activator for DC, shown by upregulated co-stimulatory molecules and enhanced cytokine/chemokine secretion. Compared to PDMS, PTFE only induced a moderate DC response. These results may explain the frequently observed inflammatory events associated with the implantation of these polymers. However, additional studies investigating the subsequent effects on T cell proliferation and polarization as well as the receptors involved in mediating the DC activation need to be performed.

Acknowledgements

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