The effects of cold atmospheric plasma on cell adhesion, differentiation, migration, apoptosis and drug sensitivity of multiple myeloma

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ABSTRACT

Cold atmospheric plasma was shown to induce cell apoptosis in numerous tumor cells. Recently, some other biological effects, such as induction of membrane permeation and suppression of migration, were discovered by plasma treatment in some types of tumor cells. In this study, we investigated the biological effects of plasma treatment on multiple myeloma cells. We detected the detachment of adherent myeloma cells by plasma, and the detachment area was correlated with higher density of hydroxyl radical in the gas phase of the plasma. Meanwhile, plasma could promote myeloma differentiation by up-regulating Blimp-1 and XBP-1 expression. The migration ability was suppressed by plasma treatment through decreasing of MMP-2 and MMP-9 secretion. In addition, plasma could increase bortezomib sensitivity and induce myeloma cell apoptosis. Taking together, combination with plasma treatment may enhance current chemotherapy and probably improve the outcomes.

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1. Instruction

Multiple myeloma (MM) is an incurable B cell malignance characterized by the accumulation of malignant plasma cell in patients’ bone marrow (BM), secretion of a unique monoclonal paraprotein, development of osteolytic bone lesions and induction of neutropenic anemia, aberrant angiogenesis, amyloidosis and hypercalcemia [1–3]. It accounts for 1% of all cancer-related deaths and approximately 10% of hematological cancers in the world [3,4]. For patients with symptomatic MM who are younger than 65 years, high-dose chemotherapy with autologous stem cell transplantation (ASCT) is the first option for treatment [5–8]. For others not eligible for ASCT, they generally receive melphalan combination with prednisone (MP) plus bortezomib (Velcade, MPV) or thalidomide (MPT) or lenalidomide (Revlimid, MPR) for initial therapy [9–13]. Although these new therapies increase response rate and prolong the overall survival compared to traditional chemotherapy used before, MM patients will relapse and become resistant to chemotherapy. Thus, new technologies and drugs need to be developed to improve myeloma clinical outcomes.

Cold atmosphere plasma (CAP), which is a novel technology developed in recent years, is an ionized gas composed of electrons, photons, charged particles and reactive species. It can be conveniently generated at atmosphere environment with the gas temperature as low as room temperature, which makes it possible for application in the medical and biological purpose. Due to the high activity of various reactive species produced by plasma, CAP shows promising prospects in disinfection, wound healing, tissue ablation, coagulation and cancer treatment [14–22]. Many groups have reported tumor cell apoptosis by plasma treatment, including hepatoma carcinoma cells, colorectal cancer cells, lung cancer cells, leukemia cells, melanoma cells, cervical cancer cells, glioma cells.

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and pancreatic cancer cells [23–32]. From pathological physiology, many aspects may affect the treatment efficiency and disease prognosis. So more and more researchers investigated other biological functions induced by CAP treatment. It was reported that plasma could increase cell proliferation in osteoblasts cells and endothelial cells [33,34]. Plasma could decrease cell adhesion in melanoma cells and liver cancer cells [35,36], while plasma treated polymer plates could facilitate cells to attach on it [37]. Several studies reported the increase of cell membrane permeability by plasma treatment, which was applied in transferring exogenous molecules into mammalian cells [38–41]. Besides, some groups demonstrated that plasma treatment could decrease cell migration rate and affect tumor cell invasion [42,43]. The biological effects of plasma on multiple myeloma has not been studied yet. In this study, we found plasma could induce myeloma cell detachment. Interestingly, the detachment area was correlated with higher hydroxyl radical density detected by emission spectrometer and mass spectrometer. Meanwhile, we found for the first time that plasma could induce cancer cell differentiation. In addition, we reported the effects of plasma on myeloma migration, drug sensitivity and cell apoptotic protein. Our results illustrated multiple functions of plasma in myeloma biology, which provided new evidences that plasma could be applied as a novel technique in cancer treatment.

2. Materials and methods

2.1. Plasma generation system

The CAP generation system used in this study is described in our previous studies [44]. It consists of a high-voltage AC power supply, gas source, gas flow controller, and oscilloscope as well as the plasma jet device. The plasma jet has a 1.0 mm powered tungsten needle enclosed in a quartz tube and a grounded outer electrode wrapped around a 6.0 mm diameter dielectric tube [44]. The working condition is He gas flow with a power supplied at 10 kHz.

2.2. RPMI culture

RPMI8226 and LP-1 MM cell line were used in this study. Cells were kindly donated by doctor Hu from Department of Molecule and Genetics, medical school of Xi’an Jiaotong University. Cells were grown in Roswell Park Memorial Institute (RPMI) 1640 medium supplemented with 10% foetal calf serum, 100 U/mL penicillin, and 50 μg/mL streptomycin (Corning, Ithaca, NY, USA). Cells were cultured at 37 °C in an incubator (Thermo Scientific Varioskan Flash, Waltham, MA, USA) containing 5% CO2. Cells were refreshed 24 h before performing experiments.

2.3. Cell viability assay

A CellTiter-Glo assay (Promega, Madison, WI, USA) was used to assess cell viability, based on the quantification of ATP. Briefly, 100 μL cell suspension was added to 100 μL luminescent reagent in a 96 well non-transparent plate. To fully induce cell lyses, the 96-well plate was placed on an orbital shaker for 2 min and then the cells were incubated at room temperature for 10 min. The luminescence intensity was recorded using the microplate reader (Thermo Scientific Varioskan Flash, Waltham, MA, USA) with the protocol of “luminometric” measurement (set the measurement time to 1000 ms without choosing any wavelength).

2.4. Optical emission spectroscopy

The emission spectra of the plasma were measured using a UV/Visible spectrometer (Ocean Optics, Dunedin, USA) within a wavelength range from 200 nm to 800 nm. The emission spectra of He plasma was analyzed in the vertical direction of the plasma jet, 2.0 cm away from the plasma jet.

2.5. Mass spectrometry

Gas plasma composition is determined by mass spectrometry. We detected the positive iron using the SIMS mode. First we scanned all the positive ions by scanning m/z from 1 to 50. Then we fixed the m/z (such as m/z = 28, N2) to dynamically detect each unique ion. We could get the distribution in radial direction of the plasma jet by shifting the jet at constant speed. Energy scanning is from 0 to 100 eV, the energy solution is 0.5 eV. The density of each ion was calculated according to the signal detected by spectrometry.

2.6. FACS analysis

The apoptosis of LP-1 cells after plasma treatment was detected by flow cytometry using an Annexin-V/PI apoptosis kit (BD). After plasma treatment for 24 h, cells were harvested and washed twice with Dulbecco’s PBS without calcium and magnesium (Corning). Cells were resuspended in 50 μL 1 × binding buffer (0.01 M Heps/NaOH (pH 7.4), 0.14 M NaCl, 2.5 mM CaCl2) with 2 μL annexinV-APC (3 μg/mL) and 2 μL PI (50 μg/mL) and incubated at room temperature in the dark for 15 min. An additional 400 μL 1 × binding buffer was added and samples were analyzed by flow cytometry. CD138 expression was detected by anti-CD138-PE (BD). Cells were suspended in 50 μL PBS with 1 μL CD138-PE for 30 min, cells were washed and analyzed by flow cytometry.

2.7. Real-time PCR analysis

Total RNA was prepared with EZNAR total RNA Kit II (Omega Bio-Tec Inc., Doraville, GA, USA) following manufacturer’s instructions and quantified in Nano Drop spectrophotometry (BioTek® Instruments Inc., Winooski, VT, USA). First strand cDNA was synthesized by RevertAid first strand cDNA synthesis kit (Thermo Scientific, Waltham, MA, USA), and the reactions were carried out on Applied Biosystems Veriti™ Thermal Cycler (Applied Biosystems, Foster City, CA, USA). Real-time PCR were performed on Bio-Rad CFX Connect™ Real-time System (Bio-Rad, Foster City, CA, USA). Primer sequences for real-time PCR.

<table>
<thead>
<tr>
<th>Gene-name</th>
<th>5’-3’ sequence</th>
<th>Product (bp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>XBP-1</td>
<td>Forward CTCGAGTCCGAGCCAGGTGT</td>
<td>218</td>
</tr>
<tr>
<td></td>
<td>Reverse GGCGTGGTAAAGAANCTGGGT</td>
<td>210</td>
</tr>
<tr>
<td></td>
<td>Reverse GAACCGAAGTACGGCCATCA</td>
<td>349</td>
</tr>
<tr>
<td>EBF</td>
<td>Forward CCCAGAAATTGCTGGCCATCT</td>
<td>233</td>
</tr>
<tr>
<td>CD56</td>
<td>Reverse TCGTTTCTGTCCAGGGCAC</td>
<td>195</td>
</tr>
<tr>
<td>CD44</td>
<td>Reverse CACACACCCCTTCCATACCAC</td>
<td>264</td>
</tr>
<tr>
<td>CD45</td>
<td>Reverse TGGTGCTTTAATCTTGGGCA</td>
<td>101</td>
</tr>
<tr>
<td>CD11a-Mnp</td>
<td>Forward GGGTTTCCCTGCAAAT</td>
<td>478</td>
</tr>
<tr>
<td></td>
<td>Reverse CATACGCCCCCATCTGACGAACCAG</td>
<td>250</td>
</tr>
</tbody>
</table>
USA), the total reaction volume was 20 µL containing: 1) 10 µL 2 × QuantiFast SYBR Green PCR MasterMix (Qiagen, Hilden, NRW, Germany); 2) 1 µL DNA template (<100 ng/reaction); 3) 1 µL of 10 µM forward and reverse primers respectively (final concentration was 0.5 µM). 4) 8 µL H2O. The primers used for the real-time PCR were listed in Table 1. The optimized amplification protocol consisted of one cycle of 95 °C for 5 min and then 38 cycles of 95 °C for 10 s, 60 °C for 30 s. The melting curves were obtained by slow heating (0.5 °C/s) at temperatures from 60 °C to 95 °C. All samples were run in duplicate. The relative expression of target genes were normalized by β-actin as a housekeeping gene. Furthermore, to verify the results of amplification, we tested the products by gel electrophoresis on 1.5% (w/v) agarose with GelRed (Biotium, Hayward, CA, USA). Images of stained agarose gel were captured using BioDoc-ItTM Imaging System (UVP, Cambridge, UK).

2.8. Combination effect of bortezomib and plasma treatment

Bortezomib (MedChem Express, Princeton, NJ, USA), known as a potent 20 S proteasome inhibitor, was dissolved in dimethylsulfoxide (DMSO) as a stock solution (10 mM) and diluted with DMSO to the required concentration. LP-1 cells were seeded in 96-well plates at 1 × 10^5 cells/well and then cultured in the presence of bortezomib (the final concentration of bortezomib in medium was 0, 1, 3, 5, 8, 10 and 20 nM) for 24 h and 48 h respectively. After incubation, cell viability was detected by Cell Titer-Glo as described previously. Moreover, to investigate the concerted influence of bortezomib and plasma on LP-1 cells, four treatments were performed: control group, without any treatment; bortezomib group, 3 nM and 5 nM bortezomib; plasma group, 30 s and 40 s He (2slm, 10 kV); combined group, 3 nM bortezomib + 30 s He and 5 nM bortezomib + 40 s He. Cell viability was determined after 24 h incubation.

2.9. Migration assay

Migration ability of LP-1 cells were accessed by a transwell assay (BD). Briefly, 5 × 10^4 cells in 300 µL serum-free medium were added into inserts containing 8 µm pores and allowed to migrate towards 300 µL complete medium in 24-wells at 37 °C and 5% CO2 for 48 h. Cells that migrated into bottom wells were counted and calculated to migration rate.

2.10. PathScan® stress and apoptosis signaling antibody array

The PathScan® Stress and Apoptosis Signaling Antibody Array Kit (Cell Signaling Technology Inc., Danvers, MA, USA) was used to determine relative proteins involved in plasma induced myeloma cell apoptosis. There were 19 different signaling molecules, such as Akt, JNK, Bad, p38, Chk1 and eIF2 etc., which could be detected in...
this antibody array kit. When multi-well gasket was affixed to the glass slide, 100 μL array blocking buffer was added to each well and decanted gently after 15 min incubation. Then 70 μL prepared cell lysates (total protein concentration was about 0.5 mg/mL) was added and incubated for 2 h at room temperature on an orbital shaker. After washing with 1 × array wash buffer, 75 μL 1 × detection antibody cocktail was added and incubated for another 1 h. Thereafter, the wells were washed again and followed by an addition of 75 μL 1 × HRP-linked streptavidin and the slide was incubated for 30 min. Subsequently the gasket was removed, the slide was washed briefly and covered with LumiGLO®/Peroxide reagent. The images were photographed by ChemiDoc-itTM Imaging System (UVP, Upland, CA, USA) and the spot intensities were determined using Image pro-Plus software 6.0.

2.11. Statistical analysis

All experiments were repeated at least three times. Data are presented as means ± SD. Differences between groups were evaluated using the Mann–Whitney U test. P < 0.05 was considered statistically significant.

3. Results

We produced the He plasma at 10.0 kHz with a gas flow of 4.0 SLM. The distance between the plasma jet and the medium was fixed at 2.0 cm. RPMI8226 myeloma adherent cells were treated with He plasma at different voltages with different time points. Fig. 1A showed that plasma treatment resulted in a clear cell detachment circle on the plates. Using trypan-blue staining we found that cells were dead in the centre of the plate while surrounding a blank circle without any cells. In addition, outside of the

![Figure 2](image_url)
circle the cells remained alive without being affected by plasma treatment. The detachment area was positively correlated with plasma treatment time and applied voltages as shown in Fig. 1B.

As plasma contains a mixture of various active species, we tried to detect the species distribution by emission spectrometer and figure out the principle species that affected the myeloma cells. Fig. 1C showed an overall spectrum profile of various reactive species in axial direction of the plasma jet. Several characteristic peaks (OH, N2, He, O) were marked in the figure. Next, we used the macro mobile platform to detect the characteristic species in radial direction of the plasma jet. The optic probe were shifted every 0.5 mm along the diametrical line of the plasma jet. Fig. 1D showed that all these characteristic peaks were high in the centre while reducing gradually to the edge of the jet. Interestingly, when transformed the absolute intensity to relative intensity (compared to He peak), we found that intensity of OH spike (hydroxyl radical indicator) was higher at the edge of the jet, which was correlated to cell detachment area (Fig. 1E).

We further detected the distribution of reactive species by mass spectrometer. Plasma jet was fixed on the macro mobile platform and passed though the centre pin of the mass spectrometer along the diametrical line so that we could obtain the distribution in radial direction. We could detect several species’ indicators with charge-mass ratio (m/z = 14, 16, 17, 18, 28, 30 et al.) by mass spectrometer (Fig. 1F). It showed that m/z of 14 (N⁺), 28 (N₂⁺) and 30 (NO⁺) had no difference in the centre and edge of the jet, m/z of 16 (O₂⁺) and 18 (H₂O⁺) were higher in the centre while m/z of 17 (OH⁺, hydroxyl radical indicator) was higher at the edge of the jet (Fig. 1F). The results indicated that only OH⁺ showed a higher intensity at the edge of the jet, correlated to cell detachment area.

Next, we focused on the biological effects induced by plasma in myeloma cells. We used the LP-1 suspension cells in the following experiments. Because LP-1 cells could be directly collected for detection without trypsinization or scraping, which made it more convenient and precise for further analysis. By real-time PCR we detected several adhesion molecules of myeloma cells after plasma treatment for 1 min and 2 min. It showed that CD44 and CD11a were up-regulated by plasma while CD56 and CD45 were not affected (Fig. 2A). Fig. 2B showed the corresponding bands of each gene by electrophoresis.

Blimp-1, XBP-1 and EBF are three major cell differentiation markers of myeloma cells. We investigated whether gas plasma could have an effect on myeloma cell differentiation. Real-time PCR results showed that plasma treatment for 2 min could up-regulate Blimp-1 and XBP-1 expression while EBF expression was decreased (Fig. 2C), indicating plasma could shift myeloma cells to a more differentiated status. Fig. 2D showed the corresponding bands of each gene by electrophoresis. Furthermore, we confirmed by FACS analysis (Fig. 2E) that plasma treatment could increase the percentage of the CD138⁺ cells (surface marker of differentiation).

Metastasis is a feature of MM, MMP-2 and MMP-9 are two critical factors for myeloma cell invasion. We analyzed the expression of MMP-2 and MMP-9 by real-time PCR and found that both of them were down-regulated by plasma treatment for 1 min and 2 min (Fig. 3A). Fig. 3B showed the specific PCR products of MMP-2 and MMP-9 by electrophoresis. By transwell assay, we confirmed that the migration ability of LP-1 cells was suppressed by plasma treatment for 1 and 2 min (Fig. 3C).
Meanwhile, drug resistance is one of the big challenges in myeloma therapy. Bortezomib is a first-line drug used in myeloma chemotherapy. First, we showed that cell viability was decreased gradually after bortezomib treatment for 24 h and 48 h in a dose-dependent manner (Fig. 3D). Then, we tried to investigate whether plasma could increase bortezomib sensitivity. As shown in Fig. 3E, combination of plasma treatment (30 s and 40 s) with bortezomib (3 nM and 5 nM) for 24 h could significantly decrease the myeloma cell viability compared to either plasma treatment or bortezomib treatment alone.

Lastly, we investigated the effect of plasma on myeloma cell apoptosis. Compared to the control group, myeloma cell apoptosis showed a time-dependent manner after plasma treatment for different durations as measured by annexin-V/PI staining (Fig. 4A). We further did a cell apoptosis protein array to detect the expression changes of various proteins involved in cell apoptosis signaling. The array data revealed that most of the proteins showed no difference after plasma treatment for 1 min and 2 min. While two of them, JNK was decreased but eIF2α was increased gradually after plasma treatment for 1 min and 2 min (Fig. 4B), indicating that they might be involved in plasma-induced cell apoptosis.

4. Discussion

In this study, we first found that plasma treatment could lead to cell detachment, depending on the applied voltage and the treatment time. We found the detachment area was at the edge of the plasma jet, so we detected distribution of species in the radial direction to find out whether the density of some species were higher at the edge of the jet. By emission spectrometer and mass spectrometer, we detected indicators of several species and found that the density of OH· was higher at the edge of the jet. In gas phase, OH· was mostly produced by the following reaction: 

\[ e + H_2O \rightarrow H + OH + e \]

Therefore, He plasma could produce hydroxyl radical when reacting with the vapour in the ambient environments. It also explains why the density of OH· is higher at the edge of the He plasma jet. The concentration of OH· in the liquid could be directly measured by ESR (electron spin resonance) [47], yet it is impossible to detect the distribution of OH· in the radial direction in the liquid. Besides, we demonstrated that OH· in the gas phase of the plasma could only permeate into liquid less than 0.1 mm [48], so that OH· in the gas phase of plasma could not directly affect cells in the medium. However, OH· in the gas phase may interact with liquid and convert into long-lived H2O2 or O2, mainly by the reaction of:

\[ \text{OH} \cdot + \text{H}_2\text{O} \rightarrow \text{H}_2\text{O}_2 + \text{H} \]

\[ \text{OH} \cdot + \text{H}_2\text{O} \rightarrow \text{H}_2\text{O}_2 + \text{H} \]
2OH → H$_2$O$_2$; OH$^–$ + H$_2$O$_2$ → H$_2$O + H$_2$O and HO$_2$ → O$_2$ + H$^+$ [48]. We further pointed out the possibility of OH$^–$ regeneration in situ of the cells from O$_2$ and HO$_2$ at the presence of Fe$^{3+}$ [49]. OH$^–$ is a highly reactive particle that could react with almost every biological molecule [50]. Based on these aspects, we proposed that the high density of OH at the edge of the jet might converted into O$_2$ or HO$_2$ that permeated deeper to reach the cells. And they could react with cells by regeneration of OH$^–$, thus resulting in cell detachment.

Next, we investigated the effects of plasma on adhesion molecules, cell differentiation, migration, cell apoptosis and drug sensitivity in MM cells. CD56, CD44, CD45 and CD11a are several major adhesion molecules of myeloma cells [51]. We found that plasma treatment could increase CD44 and CD11a mRNA expression, which may indirectly affect myeloma cells as CD44 and CD11a were reported to be involved in drug resistance, tumor metastasis and myeloma cell growth arrest [52–54]. Cell differentiation status of tumor cells may affect therapy outcomes as poor cell differentiation may indicate a shorter overall survival. Our results showed that Bлим-p and XBP-1 were up-regulated while EBF was down-regulated by plasma treatment, indicating that plasma could change myeloma cells to a more differentiated status [55–57], which could be a potential benefit for the chemotherapy. MMP-2 and MMP-9 were metalloproteinases that could degrade extracellular matrix (ECM) and facilitate myeloma cell invasion and migration [58,59]. It was reported that MMP-2 and MMP-9 were highly expressed in myeloma cells [60]. Plasma treatment could reduce the expression of MMP-2 and MMP-9, which results in the suppression of myeloma cell migration. In addition, we found that plasma treatment could increase the sensitivity of myeloma cells to bortezomib, which provided a new strategy to overcome drug resistance in myeloma treatment. Previous study reported that CYP1A1 was involved in bortezomib drug resistance by accelerating bortezomib metabolism in myeloma cells [61]. Whether plasma treatment of myeloma cells could decrease CYP1A1 expression thus improving the sensitivity to bortezomib needs to be further investigated. Moreover, we demonstrated that plasma treatment could induce myeloma cell apoptosis through a time dependent manner. To further analyze which proteins were involved in plasma induced cell apoptosis, a cell apoptosis protein array which includes 19 apoptosis related proteins was performed 24 h after plasma treatment of LP-1 cells for 1 min and 2 min. We found that JNK was decreased while elk2a was increased after plasma treatment. Chauhan et al. reported the JNK-dependent mitochondrial pathway during myeloma cell apoptosis [62], indicating the possibility of induction of mitochondrial apoptotic signaling by plasma treatment of myeloma cells. Another paper showed that elk2a, as an endoplasmic reticulum (ER) stress response protein [63], was increased after treatment with a proteasome inhibitor MLN9708 in myeloma cells. Along with our results, we supposed that the production of reactive species by plasma, triggered the ER stress response and induced mitochondrial associated apoptosis. In a whole, we demonstrated that CAP, as a new technology, has a multiple biological effects on myeloma cells, especially on the induction of apoptosis, stimulation of cell differentiation, increasing drug sensitivity and suppression of migration ability. These benefits of plasma treatment, showed a potential application of plasma in combination with chemotherapy to myeloma patients.

In conclusion, we found that CAP could detach the adherent myeloma cells, and the detachment area was correlated with higher density of hydroxyl radical in the gas phase of the plasma. Furthermore, plasma could promote myeloma cell differentiation and suppress the migration ability. In addition, plasma treatment could efficiently induce cell apoptosis and increase bortezomib sensitivity. These results showed the promising potential of plasma treatment in improving myeloma therapy.

**Conflict of interest**

The authors declare no conflict of interest.

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**References**


A. Majumdar, R. Ummanni, K. Schroder, R. Walther, R. Hippler, Cancer cells.


C.M. Edelblute, L.C. Heller, M.A. Malik, R. Heller, Activated air produced by plasma.

Y. Sakai, V. Khajoee, Y. Ogawa, K. Kusuhara, Y. Katayama, T. Hara, A novel mechanism.

M. Leduc, D. Guay, R. Leask, S. Coulombe, Cell permeabilization using a non-electroporation.


P. Sun, Y. Sun, H. Wu, Z.J. Lopez, W. Liu, J. Zhang, R. Li, J. Fang, Atmospheric pressure.


M. Balasubramanian, V.N. Vasilets, A.F. Gutsol, A. Fridman, G. Friedman, Cell signaling.


S. Nishimura, An epoch-making application.


M. Shapiro-Shelef, K. Calame, Plasma cell differentiation.


M. Shapiro-Shelef, K. Calame, Plasma cell differentiation and multiple myeloma.


M. Shapiro-Shelef, K. Calame, Plasma cell differentiation.


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