CD36 Gene Transfer Confers Capacity for Phagocytosis of Cells Undergoing Apoptosis
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Summary
Phagocyte recognition and ingestion of intact cells undergoing apoptosis are key events in this generally important program of cell death. Insufficient phagocyte capacity for apoptotic cells can result in failure to clear dying cells before membrane integrity is lost, resulting in leakage of noxious cell contents and severe tissue damage. However, no means has been available to increase phagocytic clearance of apoptotic cells. We now report that transfection of the macrophage adhesion molecule CD36 into human Bowes melanoma cells specifically conferred greatly increased capacity to ingest apoptotic neutrophils, lymphocytes, and fibroblasts, comparable to that exhibited by macrophages. Furthermore, when CD36 was transfected into another cell type with limited capacity to take up apoptotic bodies, the monkey COS-7 cell, similar effects were observed. Therefore, CD36 gene transfer can confer "professional" capacity to ingest apoptotic cells upon "amateur" phagocytes.

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Cell clearance by apoptosis protects surrounding tissues from damage due to uncontrolled leakage of noxious contents from dying cells (1–6). Intact apoptotic cells can be taken up in vivo by neighboring cells, often of the same type, acting as "amateur" phagocytes. Where the load of apoptotic cells is high, as in the thymus (7) or inflamed site (3, 8), this job is done by "professional" phagocytes, macrophages, which can clear large numbers of apoptotic cells. Nevertheless, this normally efficient clearance system can fail (8, 9). A dramatic example was recently afforded by intraperitoneal administration of antibody to Fas, which triggered rapid and widespread hepatocyte apoptosis (9). However, presumably because of insufficient local capacity to clear an unphysiologically massive load of apoptotic cells, hepatocytes disintegrated and coagulative necrosis of the liver and death rapidly ensued (9). This is an important observation, because there is a growing interest in the possibility that selective triggering of apoptosis might be useful in deleting dangerous cells from the body, such as tumor cells or auto-reactive lymphocytes (10). Unless local phagocytic capacity is able to cope with a massive increase in load of apoptotic cells, such putative treatments could have dire effects on surrounding tissues. Consequently, we sought a means to confer increased capacity for uptake of apoptotic cells.

Mechanisms by which phagocytes recognize cells undergoing apoptosis are incompletely understood (6). However, mAb inhibition experiments suggested that human monocyte-derived macrophages (Mø) can employ the adhesion receptor CD36 (11, 12) in high capacity phagocytosis of apoptotic neutrophils and lymphocytes (4, 5). The data suggest that Mø CD36 cooperates with Mø αββ vitronectin receptor integrin to bind the adhesive glycoprotein thrombospondin (TSP), which then acts as a "molecular bridge" binding the Mø to the apoptotic cell (4, 5). However, a role for CD36 in phagocytosis had not been demonstrated directly. In this study we investigated whether CD36 gene transfer can confer phagocytic capacity for cells undergoing apoptosis.

Materials and Methods

Phagocytes Used in the Study. Bowes melanoma cells (gift of Dr. D. B. Rifkin, New York University Medical Center) were stably transfected as previously described (12) with PMV7 neomycin resistance vector (control) or vector incorporating CD36 cDNA and selected in medium with G418 (250 μg/ml). By flow cytometry (13, and not shown) >80% of CD36+ Bowes cells expressed CD36 at levels comparable to Mø.

COS-7 cells (from American Type Culture Collection, Rockville, MD) were transiently transfected with cdm8 vector bearing either CD36 cDNA or FcR1(p135) cDNA by standard DEAE dextran-mediated transfection, as described (12, 14). Comparable levels of CD36 and FcR1 expression were obtained. With regard to CD36, these were ~10-fold lower than the high levels of CD36 expression achieved by stable transfection of Bowes cells (not shown). In common with Bowes cells, COS-7 cells expressed epitopes bound by 23C6 αββ mAb.

Apoptotic Cells Used in the Study. In all cases, apoptotic cells were obtained by well-established protocols, had viability >95%
by trypan blue dye exclusion and typical light microscopical features of apoptosis.

Neutrophils used were prepared from normal human peripheral blood and "aged" in culture in 24 h so as to undergo apoptosis, exactly as described (3).

Lymphocytes used were a B-cell line derived from MUTU-BL Burkitt Lymphoma Group i cells (gift of J. Hickman, University of Manchester, UK; reference 15), which were triggered to undergo apoptosis by culture in serum-free RPMI medium for 48 h; nonapoptotic cells were harvested from cultures in RPMI plus 10% FCS.

Fibroblasts used were SV40-transformed murine 3T3 fibroblasts (gift of D. Ucker, Medical Biology Institute, La Jolla, CA; reference 16), and were triggered to undergo apoptosis by culture in serum-free RPMI medium for 24 h.

**Phagocytosis Assays.** Bowes cells were subcultured in DME medium plus 10% FCS as adherent monolayers in 96-well tissue culture plates, washed, and then interacted by well-established methods (3-5, 17) for 3 h with 10^5 per well apoptotic cells in the same medium. Noningested apoptotic cells were then washed away with cold saline. In some experiments, monolayers were fixed with 2% glutaraldehyde and then stained for myeloperoxidase to reveal ingested apoptotic neutrophils, as described (16). However, for quantitation of phagocytosis, the monolayer was trypsinized at the end of the interaction and a cyt centrifuge preparation made from each well, which was fixed and stained with Haemalum to reveal ingested apoptotic cells; in neutrophil experiments the cytopreps were also counterstained with myeloperoxidase. The proportion of Bowes cells ingesting apoptotic cells in each cytoprep was then determined by microscopical counting of 300 Bowes cells per slide. In some experiments, data were also presented as the number of ingested PMNs per 100 Bowes cells. In further experiments, at the end of a phagocytosis assay, trypsinized Bowes CD36+ cells were prepared for EM by standard methods.

COS-7 cells were grown in 24-well plates in RPMI 1640 medium plus 10% FCS, and then interacted with apoptotic cells by identical methods to those used for Bowes cells. COS-7 cells were assessed 48 h after transfection.

Inhibitors were included directly in the interaction medium (at the concentrations given below or in the figure legend).

**Antibodies Used in Phagocytosis Assays.** The mAbs used have all been employed before in studies of phagocyte recognition of apoptotic cells (4, 5, 18), and no mAb inhibited human Mo phagocytosis of opsonized erythrocytes in control experiments. The CD36 mAb (OKM5; IgG1; reference 19) and β1 mAb (15.4.2; IgG1; gift of M. Ginsburg, Scripps Research Institute, La Jolla, CA; reference 20) were employed at 50–100 μg/ml. mAb to Thy1.1 (OX7; used as irrelevant control IgG1; from Serotec, Banbury, UK), the αvβ3 mAb (23C6; IgG1; gift of M. Horton, St. Bartholomew's Hospital, London, UK; reference 21), the thrombospondin mAb (C6.7; IgG1; gift of V. Dixit; reference 22), a second CD36 mAb (SMo; IgM; gift of Dr. N. Hogg, Imperial Cancer Research Fund; reference 23), and a CD15 mAb (mAb 28; IgM control for SMo; gift of Dr. N. Hogg, reference 23) were used at 1:50 dilution of ascites.

**Other Inhibitors.** Phospho-t-serine (Sigma Immunochemicals, St. Louis, MO) was used at 1 mM (24, 25). Soluble CD36 was prepared as described (13, 26), and human fibronectin was from Calbiochem (Cambridge Bioscience, UK).

**Results**

**Transfection of Bowes Cells with CD36 Confers Capacity for Phagocytosis of Apoptotic Neutrophils.** The human Bowes mela-

![Figure 1. Enhanced phagocytosis of apoptotic neutrophils by Bowes melanoma cells stably transfected with CD36 (examples arrowed). (a) Appearance of washed monolayers of CD36+ (left) and vector-only control (right) Bowes cells at end of 3 h interaction with apoptotic neutrophils; ×200. Note much greater number of myeloperoxidase-positive, brown-staining apoptotic neutrophil bound by CD36+ cells; nuclei are not stained by this technique. (b) Cytocentrifuge preparation of CD36+ Bowes cells trypsinized after interaction, demonstrating phagocytosis of apoptotic neutrophils; ×1000. Note condensed chromatin of ingested cells. (c) Electron micrograph (×2000) of CD36+ Bowes cell demonstrating uptake of neutrophil with typical features of apoptosis (N).**

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CD36 Confers Capacity to Recognize Apoptotic Cells of Other Lineages. We assessed whether transfected CD36 specifically conferred increased capacity to ingest apoptotic cells other than neutrophils. CD36+ Bowes cells took up apoptotic lymphocytes significantly more avidly than Bowes cells transfected with vector alone; nonapoptotic lymphocytes were not recognized by transfectants. Furthermore, specificity of recognition of apoptotic lymphocytes was confirmed by the inhibitory effects of soluble CD36 and mAbs to CD36, TSP and \( \alpha_\beta_3 \); PSR inhibitor had no effect. (Fig. 3 a). Identical results were obtained with apoptotic fibroblasts (Fig. 3 b), demonstrating that CD36 can also confer capacity to phagocytize apoptotic cells of a nonleukocyte lineage.

Phagocytosis of apoptotic neutrophils is inhibited by soluble CD36, but not by fibronectin (Fn) control. [ ], Fn; O, CD36. (c) CD36+ Bowes cell phagocytosis of apoptotic neutrophils is inhibited by mAbs to CD36 (OKM5), \( \alpha_\beta_3 \) (23C6), \( \beta_3 \) (15.4.2.), and TSP (C6.7). Irrelevant control mAb (OX7) and phospho-t-serine, an inhibitor of macrophage PS receptors, have no effect. *p <0.05.
Table 1. Soluble CD36 Specifically Inhibits the Phagocytic Capacity of CD36 + Bowes Cells for Apoptotic Neutrophils

| Concentration | CD36 | Fibronectin |
|---------------|------|-------------|
| Nil (control) | 47 ± 8.0 | - |
| 2 µg/ml       | 27 ± 2.0 | 47 ± 6.0 |
| 5 µg/ml       | 25 ± 3.0 | 41 ± 5.5 |
| 10 µg/ml      | 19 ± 0.5* | 38 ± 2.5 |
| 20 µg/ml      | 12 ± 0.5* | 37 ± 5.0 |

Data are mean ± SE, n = 6. *p <0.05 vs control.

**CD36 Transfection Also Confers Phagocytic Capacity upon COS-7 Cells.** To establish that the ability of transfection with CD36 to confer capacity for phagocytosis of apoptotic cells upon Bowes cells was not an idiosyncrasy of this cell type, we transiently transfected COS-7 cells with cdm8 vector incorporating CD36 cDNA (12, 14). Despite yielding ~10-fold lower levels of CD36 expression than stable transfection of Bowes cells, this conferred specifically increased capacity to phagocytize apoptotic neutrophils when compared with nontransfected COS-7 cells, or cells transfected with an irrelevant phagocytic receptor, FcR1 (Fig. 4).

**Discussion**

CD36 (also known as glycoprotein IV) is an 88-kD monomeric cell surface molecule expressed by a limited range of cell types, namely monocyte-macrophages, microvascular endothelium, mammary epithelium, platelets and megakaryocytes, and some erythroid cells (27). CD36 was originally characterized as an adhesion receptor for thrombospondin (11, 26) and collagen (28), and was later implicated in microvascular endothelial cell binding of erythrocytes parasitized by *Plasmodium falciparum* (29, 12). Our own antibody inhibi-

Table 2. CD36 + Bowes Cell Phagocytosis of Apoptotic Neutrophils Exhibits Characteristics of an αβ, δ, Vitronectin Receptor-dependent Rather Than a Phosphatidylserine Receptor-dependent Mechanism

| Inhibitor               | Number of PMNs ingested per 100 Bowes cells |
|-------------------------|---------------------------------------------|
| Nil (medium control)    | 56 ± 10.8                                   |
| OX7 (irrelevant mAb)    | 50 ± 8.7                                    |
| OKM5 (CD36 mAb)         | 17 ± 1.5*                                   |
| C6.7 (TSP mAb)          | 15 ± 5.6*                                   |
| 23C6 (αβ, mAb)          | 5 ± 2.7*                                    |
| 15.4.2 (β, mAb)         | 17 ± 2.0*                                   |
| Phospho-t-serine        | 60 ± 6.7                                    |

Data are mean ± SE, n = 6. *p <0.05 vs medium control. Inhibitors were employed as described in Materials and Methods.

Figure 3. CD36 + Bowes melanoma cells specifically phagocytize apoptotic lymphocytes and fibroblasts. (a) Specific phagocytosis of apoptotic cells from B lymphocyte line. Note inhibition by soluble CD36 (at 10 µg/ml) and mAbs to CD36 (OKM5), αβ (23C6), and TSP (C6.7), together with lack of effect of fibronectin (Fn, at 10 µg/ml) and irrelevant mAb (OX7) controls, and failure of phospho-t-serine (1 mM) to inhibit. Antibodies were used at concentrations given in Materials and Methods. Note also that nonapoptotic lymphocytes were not ingested by CD36 + Bowes cells, and that Bowes cells transfected with PMV7 vector alone exhibited minimal phagocytosis of apoptotic B cells. *p <0.05. (b) Specific phagocytosis of apoptotic transformed murine fibroblasts. The same inhibitors were used. *p <0.05.
tion experiments subsequently implied a previously unsuspected role for macrophage CD36 in mediating phagocytosis of apoptotic neutrophils (5) and lymphocytes (18). However, because cross-linking of macrophage CD36 was known to elicit signals such as superoxide generation (30), it remained possible that such effects of CD36 mAbs might mediate spurious inhibition of Mo phagocytosis of apoptotic neutrophils. The current data are therefore the first direct demonstration that the functional repertoire of CD36 includes the capacity to promote efficient phagocytosis of apoptotic cells.

This observation is also of potential importance because it is the first example of a gene transfer strategy by which clearance of apoptotic cells could be increased. As understanding of the mechanisms by which apoptotic cells are phagocytized grows, genes other than CD36 may be found to have similar capacity to promote clearance of cells being eliminated by this mechanism. If treatments are developed which induce apoptosis in undesirable cells (10), then it may be possible to bolster local phagocytic capacity against a massively increased load of dying cells by targeting phagocytic genes to such sites. Because of its limited tissue distribution, CD36 holds some promise as a tool for promoting clearance of apoptotic cells in vivo. However, it will be important to understand the molecular mechanisms of CD36-potentiated phagocytosis, which should include detailed investigation of functional cooperation with the αvβ3 vitronectin receptor integrin and thrombospondin as observed in human Mo and CD36+ Bowes cells.

Finally, the current findings emphasize that the biological role of CD36 is not merely limited to that of an adhesion molecule. Recently, CD36 has been implicated in endocytosis of oxidized low density lipoprotein (31, 32) and fatty acids (33), and in phagocytosis of retinal photoreceptor outer segments (34). Whether CD36 has a wider role in phagocytosis and endocytosis is worth further investigation.

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References

1. Wyllie, A.H., J.F.R. Kerr, and A.R. Currie. 1980. Cell death: the significance of apoptosis. Int. Rev. Cytol. 68:251–306.
2. Raff, M.C. 1992. Social controls on cell survival and cell death. Nature (Lond.). 356:397–400.
3. Savill, J.S., A.H. Wyllie, J.E. Henson, M.J. Walport, P.M. Henson, and C. Haslett. 1989. Macrophage phagocytosis of aging neutrophils in inflammation. Programmed cell death in the neutrophil leads to its recognition by macrophages. J. Clin.
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4. Savill, J., I. Dransfield, N. Hogg, and C. Haslett. 1990. Vitronectin receptor-mediated phagocytosis of cells undergoing apoptosis. *Nature (Lond.)* 343:170-173.

5. Savill, J., N. Hogg, Y. Ren, and C. Haslett. 1989. Thrombospondin cooperates with CD36 and the vitronectin receptor in macrophage recognition of neutrophils undergoing apoptosis. *J. Clin. Invest.* 90:1513-1522.

6. Savill, J., V. Fadok, P. Henson, and C. Haslett. 1993. Phagocyte recognition of cells undergoing apoptosis. *Immunol. Today.* 14:131-136.

7. Suri, C.D., and J. Sprent. 1994. T-cell apoptosis detected in situ during positive and negative selection in the thymus. *Nature (Lond.)* 372:100-103.

8. Haslett, C. 1992. Resolution of acute inflammation and the role of apoptosis in the tissue fate of granulocytes. *Clin. Sci.* 83:639-648.

9. Ogasawara, J., R. Watanabe-Fukunaga, M. Adachi, A. Matsuzawa, T. Kasugai, Y. Kitamura, N. Itoh, T. Suda, and S. Nagata. 1993. Lethal effect of the anti-Fas antibody in mice. *Nature (Lond.)* 364:806-809.

10. Carson, D.A., and J.M. Riberio. 1993. Apoptosis and disease. *Science (Wash. DC).* 267:16607-16612.

11. Carson, D.A., and J.M. Riberio. 1993. Apoptosis and disease. *Lancet.* 341:1251-1254.

12. Asch, A.S., J. Barnwell, R.L. Silverstein, and R.L. Nachman. 1993. Apoptosis and disease. *Lancet.* 341:1251-1254.

13. Savill, J., I. Dransfield, N. Hogg, and C. Haslett. 1990. Resolution of acute inflammation and the role of apoptosis in the tissue fate of granulocytes. *Clin. Sci.* 83:639-648.

14. Savill, J., V. Fadok, P. Henson, and C. Haslett. 1993. Phagocyte recognition of cells undergoing apoptosis. *Immunol. Today.* 14:131-136.

15. Savill, J., N. Hogg, Y. Ren, and C. Haslett. 1989. Thrombospondin cooperates with CD36 and the vitronectin receptor in macrophage recognition of neutrophils undergoing apoptosis. *J. Clin. Invest.* 90:1513-1522.

16. Savill, J., V. Fadok, P. Henson, and C. Haslett. 1993. Phagocyte recognition of cells undergoing apoptosis. *Immunol. Today.* 14:131-136.

17. Savill, J., I. Dransfield, N. Hogg, and C. Haslett. 1990. Resolution of acute inflammation and the role of apoptosis in the tissue fate of granulocytes. *Clin. Sci.* 83:639-648.

18. Savill, J., I. Dransfield, N. Hogg, and C. Haslett. 1990. Resolution of acute inflammation and the role of apoptosis in the tissue fate of granulocytes. *Clin. Sci.* 83:639-648.

19. Ogasawara, J., R. Watanabe-Fukunaga, M. Adachi, A. Matsuzawa, T. Kasugai, Y. Kitamura, N. Itoh, T. Suda, and S. Nagata. 1993. Lethal effect of the anti-Fas antibody in mice. *Nature (Lond.)* 364:806-809.

20. Fadok, V.A., D.R. Voelker, P.A. Campbell, J.J. Cohen, D.L. Bratton, and P.M. Henson. 1992. Exposure of phosphatidylserine on the surface of apoptotic lymphocytes triggers specific recognition and removal by macrophages. *J. Immunol.* 148:2207-2216.

21. Fadok, V.A., J.S. Savill, C. Haslett, D.L. Bratton, P.A. Campbell, and P.M. Henson. 1992. Different populations of macrophages use either the vitronectin receptor or the phosphatidylserine receptor to recognize and remove apoptotic cells. *J. Immunol.* 149:4029-4035.

22. Ogasawara, J., R. Watanabe-Fukunaga, M. Adachi, A. Matsuzawa, T. Kasugai, Y. Kitamura, N. Itoh, T. Suda, and S. Nagata. 1993. Lethal effect of the anti-Fas antibody in mice. *Nature (Lond.)* 364:806-809.

23. Savill, J., I. Dransfield, N. Hogg, and C. Haslett. 1990. Resolution of acute inflammation and the role of apoptosis in the tissue fate of granulocytes. *Clin. Sci.* 83:639-648.

24. Savill, J., I. Dransfield, N. Hogg, and C. Haslett. 1990. Resolution of acute inflammation and the role of apoptosis in the tissue fate of granulocytes. *Clin. Sci.* 83:639-648.

25. Fadok, V.A., J.S. Savill, C. Haslett, D.L. Bratton, P.A. Campbell, and P.M. Henson. 1992. Different populations of macrophages use either the vitronectin receptor or the phosphatidylserine receptor to recognize and remove apoptotic cells. *J. Immunol.* 148:2207-2216.

26. Ogasawara, J., R. Watanabe-Fukunaga, M. Adachi, A. Matsuzawa, T. Kasugai, Y. Kitamura, N. Itoh, T. Suda, and S. Nagata. 1993. Lethal effect of the anti-Fas antibody in mice. *Nature (Lond.)* 364:806-809.

27. Fadok, V.A., J.S. Savill, C. Haslett, D.L. Bratton, P.A. Campbell, and P.M. Henson. 1992. Different populations of macrophages use either the vitronectin receptor or the phosphatidylserine receptor to recognize and remove apoptotic cells. *J. Immunol.* 149:4029-4035.

28. Fadok, V.A., J.S. Savill, C. Haslett, D.L. Bratton, P.A. Campbell, and P.M. Henson. 1992. Different populations of macrophages use either the vitronectin receptor or the phosphatidylserine receptor to recognize and remove apoptotic cells. *J. Immunol.* 148:2207-2216.

29. Ogasawara, J., R. Watanabe-Fukunaga, M. Adachi, A. Matsuzawa, T. Kasugai, Y. Kitamura, N. Itoh, T. Suda, and S. Nagata. 1993. Lethal effect of the anti-Fas antibody in mice. *Nature (Lond.)* 364:806-809.

30. Fadok, V.A., J.S. Savill, C. Haslett, D.L. Bratton, P.A. Campbell, and P.M. Henson. 1992. Different populations of macrophages use either the vitronectin receptor or the phosphatidylserine receptor to recognize and remove apoptotic cells. *J. Immunol.* 148:2207-2216.

31. Ogasawara, J., R. Watanabe-Fukunaga, M. Adachi, A. Matsuzawa, T. Kasugai, Y. Kitamura, N. Itoh, T. Suda, and S. Nagata. 1993. Lethal effect of the anti-Fas antibody in mice. *Nature (Lond.)* 364:806-809.

32. Fadok, V.A., J.S. Savill, C. Haslett, D.L. Bratton, P.A. Campbell, and P.M. Henson. 1992. Different populations of macrophages use either the vitronectin receptor or the phosphatidylserine receptor to recognize and remove apoptotic cells. *J. Immunol.* 148:2207-2216.

33. Ogasawara, J., R. Watanabe-Fukunaga, M. Adachi, A. Matsuzawa, T. Kasugai, Y. Kitamura, N. Itoh, T. Suda, and S. Nagata. 1993. Lethal effect of the anti-Fas antibody in mice. *Nature (Lond.)* 364:806-809.

34. Fadok, V.A., J.S. Savill, C. Haslett, D.L. Bratton, P.A. Campbell, and P.M. Henson. 1992. Different populations of macrophages use either the vitronectin receptor or the phosphatidylserine receptor to recognize and remove apoptotic cells. *J. Immunol.* 148:2207-2216.

35. Ogasawara, J., R. Watanabe-Fukunaga, M. Adachi, A. Matsuzawa, T. Kasugai, Y. Kitamura, N. Itoh, T. Suda, and S. Nagata. 1993. Lethal effect of the anti-Fas antibody in mice. *Nature (Lond.)* 364:806-809.

36. Fadok, V.A., J.S. Savill, C. Haslett, D.L. Bratton, P.A. Campbell, and P.M. Henson. 1992. Different populations of macrophages use either the vitronectin receptor or the phosphatidylserine receptor to recognize and remove apoptotic cells. *J. Immunol.* 148:2207-2216.
