The concept that cells can directly communicate with, and influence the function of other cells by transfer of particulate complexes or cell surface proteins (eg, antigen-bound MHC-II, integrin, ATPase channels)\(^1\) rather than soluble factors like cytokines and chemokines has excited cell biologists for decades. Extensive efforts have been made to prove the existence of this phenomenon and understand the mechanisms by which cells (especially immune cells) transfer proteins between each other. There is now evidence for at least four ways that this transfer could occur—proteolytic cleavage of the protein from one cell with attachment to another, formation of tubules between two cells, direct cell membrane fusion and transfer of enclosed membrane vesicle (figure 1). An exosome is an example of such a membrane vesicle and is significant in that it can contain the contents of both intracellular endosomes and proteins expressed on the cell membrane of its parent cell. Therefore, it could be viewed as a ‘mini-cell’, but with the added capacity to transfer the cell content or surface proteins onto another cell.

With the acknowledgement that exosomes exist and can transfer cellular material, the focus has shifted to showing that this phenomenon has functional consequences. Interest was roused when several investigators began showing that peptide—MHC complexes on exosomes can be captured by dendritic cells, which then trigger CD4 and CD8 T-cell responses.\(^5\)–\(^7\) Depending on the kind of T cells engaged by these complexes, the result could be amplification of the T-cell response or suppression, for example, if regulatory T cells were involved. Therefore, exosomes could also influence the net outcome of a lymphocyte response during infection or inflammation. The ability of exosomes to trigger immune response has been utilised in the field of tumour immunology. At least two phase I clinical trials have been carried out using exosomes to enhance the body’s own immune response against tumour cells.\(^5\)\(^,\)\(^9\) Morse et al\(^9\) purified autologous, dendritic cell-derived exosomes expressing MHC-II and used these as platforms for loading of tumour-specific antigen. They showed that infusion of these autologous exosomes was safe and resulted in detectable tumour-specific T-cell response. However, it is widely acknowledged that the role of exosomes in vivo requires further clarification. Production of exosomes is widespread and the factors controlling its relative concentration in different cells is critical and can affect many stages of an immune response.\(^1\) Nat Rev Immunol 2007;7:236–46.

**REFERENCES**

Figure 1  Potential mechanisms for intercellular protein transfer. (A) Proteins could be uprooted from the membrane of cells. (B) Proteolytic cleavage could facilitate intercellular transfer of protein ectodomains. (C) Transfer could be mediated by enclosed membrane bodies, vesicles or larger organelles at intercellular contacts. This process could involve the secretion of specialised vesicles such as exosomes. (D) Intercellular membrane fusion could produce small membrane bridges that allow protein transfer. (E) Membrane nanotubes, perhaps derived from membrane fusion or membrane bridges at the site of intercellular contact, could facilitate protein transfer between distal cells. Reprinted with permission from Macmillan Publishers Ltd. Davis DM. Nature Reviews Immunology 2007;7:238–43, copyright (2007).
Exosomes in lungs of patients with sarcoidosis: a contributor to immune pathogenesis or just another by-product of heightened immune activity?
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