example, human monocytes cultured in collagen gels show both antigenic and morphological differences compared with those on glass[11]. Monocytes and macrophages possess distinct receptors for fibronectin, laminin and possibly other extracellular components. These receptors mediate adhesion to matrix components and in the long-term may also affect specific differentiation pathways through gene activation.

Interestingly, addition of fibronectin or laminin to cultured human monocytes rapidly stimulates phagocytosis of opsonized particles via indirect effects on other plasma membrane receptors[12,13]. The long-term effects of these glycoproteins on macrophage function have not been investigated.

In conclusion, despite the paucity of direct evidence it nevertheless seems likely that the extracellular matrix is an important determinant of resident tissue macrophage heterogeneity and function. But the composition of extracellular matrix varies considerably amongst different tissues, and for optimal maintenance of differentiation, certain specialized cell types such as hepatocytes are known to require a natural 'biomatrix' extracted from liver[14]. In this respect it is worth noting that the IBT product (see Box 1) is secreted by endothelial cells and therefore closely resembles basement membrane; it contains laminin as well as collagens, fibronectin and proteoglycans. Hopefully other tissue forms of extracellular matrix will soon be available because these should provide parasitologists with invaluable tools for *in vitro* investigations of macrophage–parasite interactions.

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...ALTERNATE ANSWERS

Indigestible Phytoplankton for Mosquito Control

G.G. Marten

The shortcomings of mosquito control using pesticides have stimulated an interest in biological control as an alternative. Biological control usually brings to mind the introduction of natural enemies, but biological introductions that modify the biota of breeding areas to make them unsuitable for mosquito larvae may prove equally worthy of attention. One way to modify mosquito breeding habitats is to eliminate the food supply for mosquito larvae. Phytoplankton could play a key role in this approach because they are the principal food for many species of filter-feeding larvae.

The key lies in a long-standing observation that mosquito larvae are sometimes absent from places that appear to be ideal breeding sites. More than fifty years ago, mosquito biologists mounted an international scientific effort to find out why, directing particular attention to the kinds of phytoplankton in the water[1–3]. However, no clear relationship was found, the puzzle remained unsolved, and the matter was dropped for many years. Only recently has the question been reopened by the finding that certain species of planktonic green algae can kill mosquito larvae[4].

Mosquito larvae can digest most species of phytoplankton, but a recent study at the Hawaii Institute of Marine Biology suggests there are approximately 200 species of algae, all in the order Chlorococcales[5], that kill mosquito larvae because the larvae are unable to digest them[6]. These algae are indigestible to larvae of *Aedes*, *Anopheles*, and *Culex*, because the cell walls of the algae contain a thin layer of sporopollenin[7], a caratonoid that protects the algae from digestive enzymes. The mosquito larvae cannot discriminate between these algae and other phytoplankton, so wherever these Chlorococcales are more abundant than other phytoplankton; the larvae simply feed upon the indigestible algae until they starve to death. Many species of algae in the genera *Scenedesmus*, *Kirchneriella*, *Coelastrum*, *Selenastrum*, *Dactylococcus*, *Elakotothrix*, *Tetrallantos*, and *Tetradesmus* are known to be indigestible, and so may be at least some species in closely related genera such as *Dictyosphaerium*, *Nephrocytium*, *Nephrochlamys*, *Franceia*, and *Botryococcus* (Fig. 1).

Mosquito larvae fail to develop in small water bodies where indigestible phytoplankton predominate. But this situation is not very common in nature, so a key question for mosquito control is how to establish indigestible phytoplankton in the numerous situations where they do not occur naturally. Preliminary experiments show that indigestible phytoplankton can be substituted for those species already in the water[6], particularly when introducing local strains that are adapted to local environmental conditions. Moreover, the replacement process can be facilitated and sustained by simultaneously introducing selected species of filter-feeding zooplankton, such as *Daphnia*, whose grazing on phytoplankton gives a competitive advantage to less digestible species.

Mosquito-indigestible phytoplankton appear to have no undesirable environmental side effects. They are not toxic and can be digested by any species of aquatic animals that can break their cell walls mechanically. There is normally a diverse and abundant fauna associated with these phytoplankton in nature, and the mosquito-indigestible phytoplankton can support substantial populations of certain natural enemies of mosquito larvae such as cyclopoid copepods[4]. Thus populations of mosquito-indigestible phytoplankton, filter-feeding zooplankton, and natural enemies of mosquitoes, could be introduced and mutually reinforce each other while excluding mosquito larvae.

A major advantage of phytoplankton for mosquito control is the expectation that mosquitoes will not evolve resistance to their use. Mosquitoes have displayed an impressive ability to evolve physiological and behavioral resistance to almost any

chemical pesticide in large-scale use, and the same could happen with microbial pesticides based on *Bacillus thuringiensis*, or with biological control based on mosquito predators, parasites, or pathogens. In contrast, there is no evidence that mosquitoes can evolve resistance to the removal of resources necessary for nutrition or physical survival. Mosquito larvae would have to evolve major structural modifications to break the cell walls of these algae in order to digest them.

I do not know whether mosquito-indigestible phytoplankton will prove practical for large-scale mosquito control, but they merit further study. Such phytoplankton will be effective only for mosquito species that are primarily filter feeders, and only where these phytoplankton can predominate over other food in the water column. I do not know for how many breeding habitats, or for how many species of mosquitoes, this would be the case. Nor do I know how long these phytoplankton, once established, can maintain themselves under various field conditions, though they sometimes have persisted for a year in small-scale field experiements in Hawaii. The next step is to culture local strains of these phytoplankton, and introduce them in coordination with mutually reinforcing organisms to a variety of mosquito breeding habitats. Such integrated control could be highly beneficial, both to ourselves and to the environment.

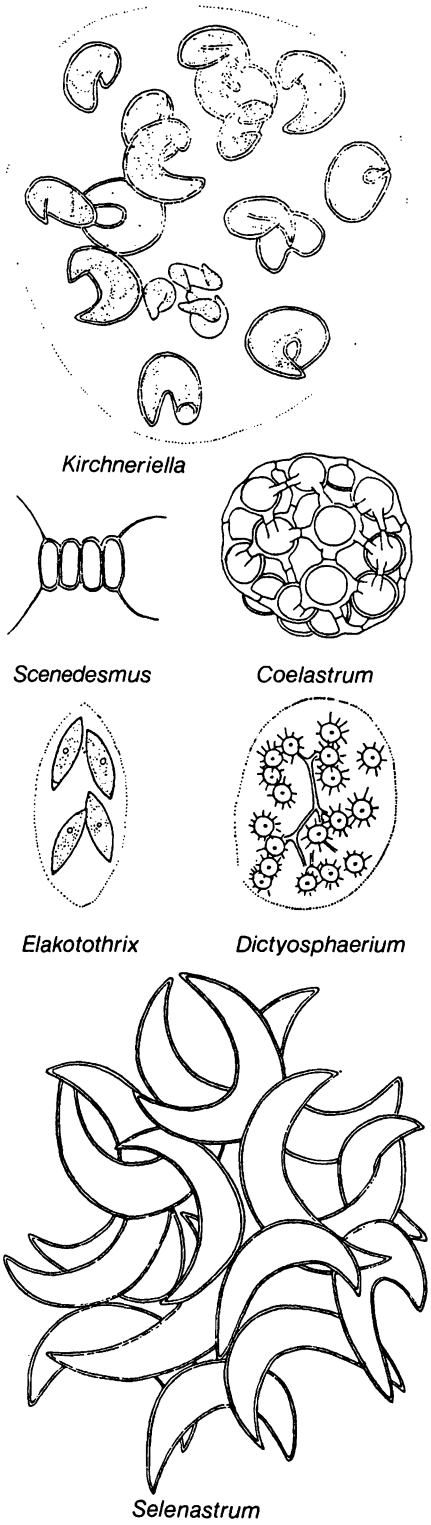
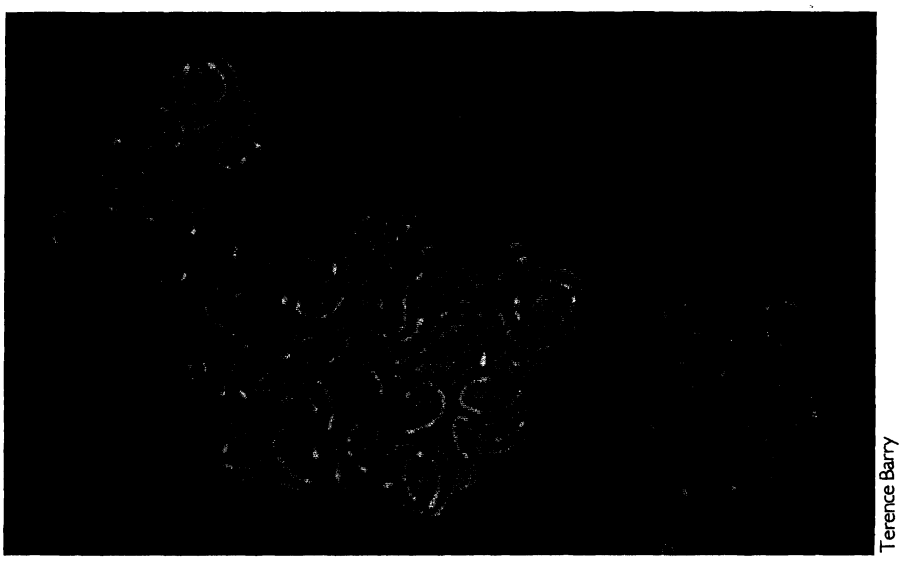


Fig. 1. Common phytoplankton which is indigestible to mosquito larvae. Kirchneriella, Coelastrum, Elakotothrix *and* Dictyosphaerium *cells are enclosed in a gelatinous matrix which holds the cells together, although it plays no part in their indigestibility.*



Terence Barry

Fig. 2. Kirchneriella irregularis (x1200). *The green algal cells are held together by a gelatinous matrix which has been highlighted in this picture by adding indian ink to the water.*

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