Ancient food for thought

Warwick Bray

Archaeological evidence of unexpected modes of food production in the tropics of lowland Central and South America carries lessons for modern farmers and students of crop-plant evolution.

In the debate about how to make rational, sustainable use of the American tropics, some of the more enlightened governments are taking a hard look at indigenous farming practices. Two papers (one on page 190 of this issue[1], the other in the 19 October issue of *Nature*[2]) show that archaeologists have a great deal to contribute by revealing crop regimes and forms of land management that have no counterparts today.

The conventional view that seasonally flooded savannas are worthless for cultivation and are suitable only for cattle ranching has been overturned by Erickson's work[1] in the Bolivian Amazon (Fig. 1). He has used aerial photographs and ground surveys to map a 'lost' prehispanic landscape of man-made earthworks, with settlement mounds, causeways, raised and drained fields, and also 500 km^2 of weirs and artificial ponds — which, he argues, were used for fish harvesting on a massive scale.

Erickson does not say whether the Bolivian government plans to reactivate the fish weirs, but experiments have already begun with his raised fields[3]. The archaeological sites yielded pollen of edible tubers (*Xanthosoma* species), and both maize and manioc (cassava) did well on the modern experimental plots. Several older farmers told Erickson it was the first time they had seen the pampas produce agricultural crops. Similar, and successful, experiments have been carried out with high-altitude raised fields in the Titicaca basin.

This may be just the start of things. In the savannas of Caribbean Colombia there are 5,000 km^2 of abandoned prehispanic fields and canals, unknown until the 1960s, and there are other, smaller expanses of raised fields in Mexico, Guatemala, Belize, Venezuela, Surinam, Guyana, Ecuador and Peru. Written documents from post-conquest times say nothing about the technology of these systems. But if further experiments show that the ancient agricultural landscapes can be reconstituted, and the savannas can be made productive, we may have an alternative to reckless felling of the rainforest.

Archaeological data of this kind help to resolve the dispute between historical anthropologists who accept European reports of large populations along the Amazon floodplain and in the savannas, and those members of the calorie-counting school who claim that protein scarcity imposed a limit on population growth in the lowland tropics until the introduction of European livestock. There is good evidence that a combination of game, fish, maize and palm fruits in seasonally flooded areas provides abundant protein[4]. Instead of worrying about protein, we should perhaps now think more about where the starch came from.

Figure 1 **Central and northern South America today. Erickson's paper[1] describes investigations in the Bolivian Amazon and the identification of prehispanic raised fields, as well as weirs and artificial ponds. Piperno *et al.*[2] report evidence of starch grains 5,000–7,000 years old from the Aguadulce rock shelter, Panama. Taken together with other evidence, these findings point to the early and independent development of root-crop agriculture in the lowland American tropics.**

Taking the long archaeological view, this is not a silly question, especially for the initial stages in the evolution of agriculture. In the 1970s and 1980s archaeologists began to recover pollen, phytoliths (microscopic bodies of silica found in plant cells) and carbonized plant tissue from tropical sites and, more recently, to identify tuberous-plant starch grains that are not normally preserved. Piperno and colleagues[2] report the finding of starch grains from cultivated manioc, yams, arrowroot and maize on milling stones excavated at the Aguadulce rock shelter, Panama, and dated to between 5,000 and 7,000 years ago. This is the earliest evidence for root-crop cultivation in the Americas, and raises a series of questions.

The first generation of domesticated plants will look exactly like the last generation of wild ones, so botanists will never be able to recognize the initial experiments with cultivation. In Panama, the cultivated plants had already begun to diverge from their wild prototypes. The presence of maize and manioc is also significant, as these are not native to Panama and must have been brought into cultivation elsewhere. The genetic history of maize is still controversial[5] but the consensus is that the botanical centre of origin is somewhere in Mesoamerica (Mexico and northern Central America), and most plausibly in Mexico. Manioc was probably domesticated in southwest Brazil[6]. These plants must therefore have reached Panama by a process of secondary dispersal, as domesticated crops and after a period of genetic adaptation to new ecological conditions.

The implication here is that we should be looking for a still earlier stage of tropical agriculture, without maize or manioc (the principal sources of starch today), and characterized by experimentation with whatever

was locally available. There are hints of this in the pollen and phytolith cores from the lake of La Yeguada, not far from the Aguadulce site[7]. Here, below levels with maize pollen dated to about 5,700 years ago, there is a sudden and large rise, around 11,000 years ago, of particulate charcoal and of plants typical of forest gaps. This phenomenon may well represent small-scale forest clearance for horticulture.

Like Erickson's fish farming, the earliest forms of tropical cultivation may be unlike anything that can be seen today. But recent excavations all over the lowlands point to the importance of tubers such as yams, arrowroot, sweet potato and *Xanthosoma*, and also emphasize the vital role of palm products. Arrowroot, a neglected crop today, is beginning to emerge as a significant early domesticate, with finds from highland Colombia dated to 10,000–9,000 years ago[8] and from coastal Ecuador to around 3,600 years ago[9]. All this tends to confirm what Carl Sauer[10] suggested as early as 1952: that there was an early and independent development of root-crop agriculture in the lowland American tropics, comparable in importance to the maize–beans–squash agriculture of Mesoamerica or the high Andean combination of potatoes, seed crops (quinoa) and llamas.

Perhaps we should now bury for ever the concept of 'centres of origin' for American agriculture. Unlike plants and animals, ideas are not constrained by ecological conditions. Archaeology is beginning to demonstrate the huge variety of agricultural practices in pre-European America, and also to suggest that people everywhere began by experimenting with the cultivation of plants they were already collecting in the wild. ■

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Signal transduction

A most interesting factor

Richard Bucala

The effects of the signalling molecule MIF are quite well understood, but how it works remains a mystery. Some of the pathways behind its activity have now been revealed — with surprising results.

The names — and acronyms — bestowed on proteins tend to reflect what they are doing at the time they are discovered. For example, one particular cytokine protein was found to inhibit the random migration of macrophages (immune cells that engulf foreign material) in culture. This led to it being called MIF, for 'macrophage migration inhibitory factor'. But this acronym also has another, less formal definition — 'most interesting factor'. Indeed, the functions of MIF, in the immune system and elsewhere, are diverse and intriguing. But the signal-transduction pathways underpinning MIF's activity have been unclear, so it has often been thought that this cytokine, although the first to be discovered, might turn out to be the last to be fully understood.

On page 211 of this issue, however[1], Kleemann and colleagues provide fresh insight into how MIF works, by showing that it interacts inside cells with an activator of gene expression, Jab1. The authors also propose a new, unconventional signalling mechanism to account for MIF's interaction with this protein.

Although MIF was identified in the early 1960s, the gene encoding it was not cloned until 1989 (ref. 2). Christened for its effects on macrophages, MIF is still known as a key regulator of innate and acquired immunity — the two broad categories of immune response in higher organisms. For example, it is important in inducing inflammation in response to invasion by bacteria, viruses and so on. But its biochemical and biological properties are not at all predictable[3,4].

For example, MIF is involved in regulating the activation of macrophages and T cells[3,5], in the release of insulin from the pancreas[6], and in carbohydrate metabolism[7]. The mouse counterpart of MIF is released by the anterior pituitary gland as a consequence of the systemic response to stresses[3,4].

The informal name for MIF was coined by Thierry Calandra after an attempt to block its expression by using glucocorticoids — steroid hormones thought to suppress the expression of pro-inflammatory cytokines. Surprisingly, low levels of glucocorticoids instead induced the release of MIF from macrophages[3]. MIF was then found to override or counter-regulate the suppressive effects of glucocorticoids on the expression of pro-inflammatory cytokines[3,5]. This may account for many of MIF's pro-inflammatory effects *in vivo*[3–5].

MIF is generally released from pituitary cells, macrophages and T cells. The underlying mechanism remains largely a mystery, as does the process by which extracellular MIF exerts its effects on target cells. But perhaps the most unusual feature of MIF is its enzymatic activity. The crystal structure of MIF is strikingly similar to that of several small bacterial enzymes called isomerases[8]. Nevertheless, it seems doubtful (given the kinetic values calculated) that MIF interacts naturally with any of the substrates identified for it in biochemical studies. And mutation analyses have not supported the idea that MIF needs a working catalytic site for any of its tasks in the immune system[8–10].

MIF also seems to allow cells to bypass death (apoptosis) mediated by the p53 tumour-suppressor protein[11]. So, because p53 function is often altered in tumours, MIF provides an important link between long-term inflammation and cancer. MIF is also involved in the sustained activation of cell-growth-promoting enzymes such as the ERK-1/2 family of mitogen-activated protein kinases[12], in promoting the growth of new blood vessels to nourish tumours[13], and in regulating antitumour T cells[14]. A variety of results[3–7,9–13] suggest that an interaction between MIF and a receptor on the surface of its target cells is essential for MIF's activities. But there remains scant information about what this receptor might be.

Kleemann *et al.*[1] now report an intriguing mechanism that bypasses the need for a cell-surface receptor (Fig. 1). They show that MIF binds to a cytoplasmic protein, Jab1. This protein usually induces both the phosphorylation of c-Jun, a protein involved in inducing cell growth, and the activity of AP-1, a transcription factor that activates the expression of pro-inflammatory genes. Jab1 also binds to and promotes the degradation of $p27^{Kip1}$, a protein that halts the cell-division cycle. By doing this, Jab1 can rescue serum-starved fibroblasts from growth arrest. MIF, however, inhibits Jab1, allowing levels of $p27^{Kip1}$ to rise; when overexpressed, MIF reduces the growth-promoting effects of Jab1 on fibroblast cells (Fig. 1).

The physical interaction between MIF and Jab1 also suggests a way by which MIF, by inhibiting Jab1, might control the pro-inflammatory effects of AP-1 (Fig. 1). It seems that the cellular effects of MIF may now be interpreted as anti-inflammatory.