

Plastid in human parasites

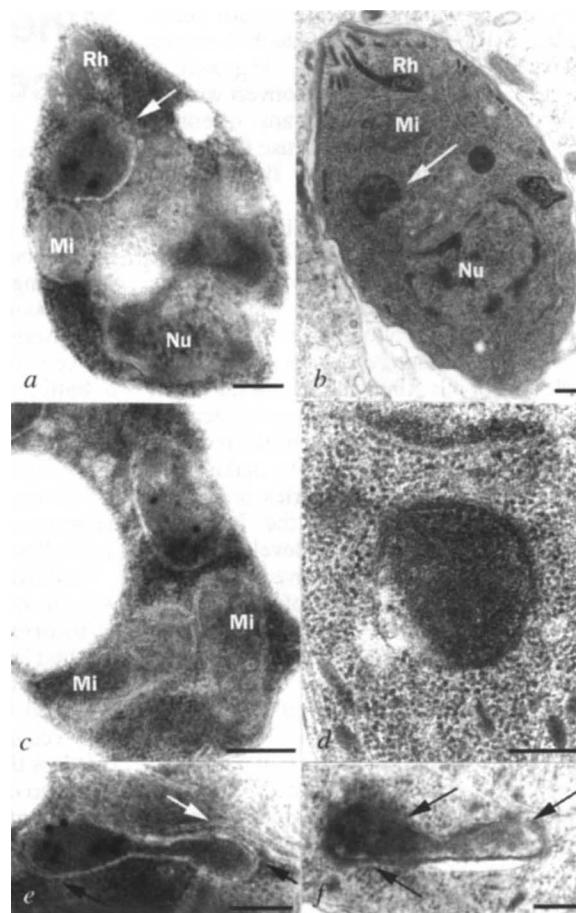
SIR — The discovery in malarial and toxoplasmodial parasites of genes normally occurring in the photosynthetic organelle of plants and algae has prompted speculation that these protozoans might harbour a vestigial plastid¹. The plastid-like parasite genes occur on an extrachromosomal, maternally inherited², 35-kilobase DNA circle with an architecture reminiscent of that of plastid genomes^{3,4}. Although the 35-kb genome is distinct from the 6–7-kb linear mitochondrial genome^{3–6}, it is not known where in the parasite cells the plastid-like genome resides.

To determine whether a plastid is present, we used high-resolution *in situ* hybridization⁷ to localize transcripts of a plastid-like 16S ribosomal RNA gene from *Toxoplasma gondii*⁸, the causative agent of toxoplasmosis. Transcripts accumulate in a small, ovoid organelle located anterior to the nucleus in the mid-region of the cell (*a, b* in the figure). We observe only one of these organelles per cell (*a–c*), except during division (endodyogeny), when an organelle is associated with each forming daughter cell (not shown). At the onset of endodyogeny, the organelle assumes a cylindrical shape (not shown) and eventually acquires a constriction, creating a dumbbell shape (*e, f* in the figure) which presumably divides into two daughter organelles. The organelle is distinct from the tubulocristate mitochondria (*c*). At least two membranes (some profiles possibly indicate a third membrane) surround the organelle (*b–f*). Certain images (*e* in the figure) reveal a layer of endoplasmic reticulum (sometimes completely) enveloping the organelle, creating a misleading impression of multiple (typically four or five) surrounding membranes.

Particles of 18 nm diameter (approximately the size of bacterium-like 70S ribosomes) are the only discernible structures within the organelle (*d, f*), the contents

being otherwise homogeneous. The 35-kb genome-containing organelle identified here did not escape the attention of early electron microscopists who — not expecting the presence of a plastid in a protozoan parasite like *Toxoplasma* — ascribed to it various names, including 'Hohlzylinder' (hollow cylinder), 'Golgi adjunct' and 'große Vakuole mit kräftiger Wandung' (large vacuole with stout surrounds) (see refs cited in ref. 9). Our preliminary experiments with *Plasmodium falciparum*, the causative agent of the most lethal form of malaria, identify an organelle (not shown) which appears similar to the *T. gondii* plastid. The number of surrounding membranes in the *P. falciparum* plastid, and its relationship to the previously described spherical body of *Plasmodium* (see ref. 9), are unknown. Our *in situ* hybridization data thus identify a third, hitherto putative, genetic compartment (a plastid) in these parasite cells. Because the plastid genome encodes components of ribosomes and the translation process^{4,10}, and we observe ribosome-like particles in it, the plastid compartment probably contains machinery to express its information content.

Toxoplasma and *Plasmodium* belong to phylum Apicomplexa, which is closely related to dinoflagellate algae (refs in ref. 3), so the parasite plastid could be a non-photosynthetic derivative of the dinoflagellate plastid (but see ref. 5). Unfortunately, no genes have yet been characterized from dinoflagellate plastids, so molecular comparison of dinoflagellate and apicomplexan plastids must wait. Whatever its origin, the presence of a plastid in apicomplexan parasites probably explains their sensitivity to certain herbicides (ref. 11 and refs therein) and drugs inhibiting plastid metabolism^{12,13}. The plastid is thus a welcome new, parasite-specific target for therapeutic agents. The role of the plastid in obligate intracellular parasites is completely unknown, but our identification of the organelle is a first step towards isolation for biochemical analysis to



a, Localization of transcripts from a plastid-like 16S rRNA gene⁸ in tachyzoite (longitudinal section) of *Toxoplasma gondii* RH by high-resolution *in situ* hybridization. Colloidal gold markers show transcripts accumulated in an ovoid compartment (arrow). Nu, nucleus; Rh, rhoptries; and Mi, mitochondria. *b*, Standard electron micrograph (embedding courtesy of D. Lindsay, Auburn University) similar to *a*, showing the plastid (arrow). *c*, Mitochondria (Mi) with tubular cristae are not labelled. *d*, Close view of plastid showing at least two surrounding membranes, homogeneous contents and ribosome-like particles (about 18 nm diameter). *e*, Dumbbell-shaped (possibly dividing), double-membrane-bound (black arrows) *Toxoplasma* plastid. Endoplasmic reticulum appressed to the plastid (white arrow) creates impression of extra surrounding membranes. *f*, Standard electron micrograph showing dumbbell-shaped *Toxoplasma* plastid with two surrounding membranes (black arrows) and ribosome-like particles (about 18 nm diameter) within. Scale bars, 0.2 μ m.

complement molecular-genetic approaches already under way^{4,10}.

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