lymerization and the attenuation of the Mg^{2+}-dependent mechanisms regulating microtubule assembly, since Al^{3+} concentrations and total aluminum burdens in these ranges become relevant under pathological conditions (*1*). In addition, the exchange of guanine nucleotides (GTP for GDP) would also be expected to be slower when Al^{3+} is associated in the GTP-tubulin ternary complex, because of the extremely slow rate of ligand exchange of Al^{3+} (about 10^{-5} the rate of that of Mg^{2+}) (*23*).

Tubulin polymerization and microtubule stability are sensitive to Ca^{2+} in vitro and in vivo, with elevated concentrations inhibiting tubulin polymerization and promoting microtubule depolymerization (*24*). The Al^{3+} microtubules were less sensitive with regard to both rate and extent of Ca^{2+}-induced depolymerization than Mg^{2+}-microtubules, and Al^{3+} (at $4.0 \times 10^{-11} M$) polymerizes significantly more tubulin in the presence of elevated Ca^{2+} concentrations than the Mg^{2+}-supported system (at 1.0 mM) (*25*). This result is presumably a consequence of the enhanced association constant of the Al^{3+}-GTP-tubulin complex relative to its Mg^{2+} counterpart and the mechanism of Ca^{2+}-mediated depolymerization in vitro (*24*); it is also consistent with slower microtubule treadmilling for Al^{3+}-microtubules relative to Mg^{2+}-microtubules.

Thus, Al^{3+} might disrupt the sensitive dynamics and thermodynamics of microtubule formation and disassembly in vivo through the inhibition of GTP hydrolysis and nucleotide exchange, as well as through a depressed sensitivity to regulation of polymerization and depolymerization processes by Ca^{2+}. In addition, Al^{3+} incorporation could affect the tertiary structure of the microtubule polymer, as well as the tubulin monomer, through the maintenance of GTP-M–bound subunits. The physiological impact of such subtle changes in microtubule structure might be manifested in altered interactions with the multiplicity of microtubule-associated proteins known to associate with both the monomeric and the polymeric tubulin subunits.

These findings may have implications for other GTP-binding proteins, which include nucleotide-binding enzymes, signal-transducing G proteins, and the product of the *ras* oncogene (*26*). The three-dimensional structures of two of these proteins incorporate a Mg^{2+} at the nucleotide-binding site (*27*). In several of these proteins, GTP hydrolysis and GDP-GTP exchange serve as critical control mechanisms (*26, 27*). The competition between Mg^{2+} and Al^{3+} may affect the normal function of these proteins in vivo.

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First Record of Giant Anteater (Xenarthra, Myrmecophagidae) in North America

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A right metacarpal III represents the first North American record of the giant anteater (*Myrmecophaga tridactyla*). Recovered in northwestern Sonora, Mexico, with a rich vertebrate fauna of early Pleistocene (Irvingtonian) age, it belongs to a cohort of large mammals that dispersed from South America to North America along a savanna corridor. Presumably habitat and climatic changes have subsequently driven this mammalian family more than 3000 kilometers back into Central America from its former expansion into temperate North America.

NEW WORLD ANTEATERS (VERMILINGUA) occur rarely in the fossil record, and knowledge of their evolution and fossil distribution have had to be pieced together (*1*). The three extant genera of the family Myrmecophagidae are presently restricted to tropical Central and South America, and the four valid fossil genera are also confined to South America. Therefore, discovery of the giant anteater (*Myrmecophaga tridactyla*) in the early Pleistocene of northernmost Mexico, more than 3000 km north of its present range, was unexpected (Fig. 1).

The fossil specimen, a complete right metacarpal III of an adult animal (Fig. 2), was recovered from the surface of (unnamed) nonmarine sediments to the northeast of El Golfo de Santa Clara, Sonora, Mexico (31°40′N, 114°30′W). It is identical in morphology, size, and proportions to the metacarpal III of modern *Myrmecophaga tridactyla*. This distinctive skeletal element, with its deep distal keel, supports the largest and most powerful digging claw that is used to open termite mounds and is quite diagnostic for this species.

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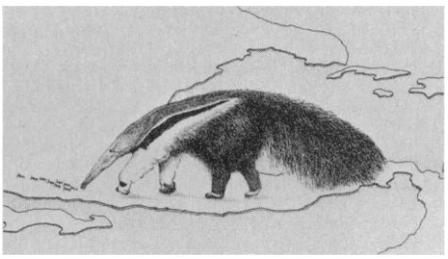

Fig. 1. The giant anteater, *Myrmecophaga tridactyla*, following the savanna corridor migration route from South America to North America. [Illustration by J. Murray]

The anteater is part of a large and varied fauna (*2*) collected from interbedded conglomerates, sandstones, and sandy siltstones of floodplain or deltaic origin. The El Golfo local fauna is early Pleistocene (Irvingtonian) in age on the basis of the joint association of *Mammuthus imperator, Megalonyx wheatleyi, Nothrotheriops* sp., and *Sigmodon curtisi* (*3*). This fauna correlates well with Irvingtonian faunas from Vallecito–Fish Creek of the Anza-Borrego Desert in southern California (*4*) and Curtis Ranch of the San Pedro Valley in Arizona (*5*).

The only previous collections of fossil *Myrmecophaga tridactyla* include a rich sample from Pleistocene cave deposits in the Minas Gerais Province, Brazil (*6*), and an isolated specimen from Uruguay (*7*), the southernmost record of this species. It is not known as a fossil from Central America, even though it currently ranges as far north as eastern Guatemala and southern Belize (*8*). The presence of *Myrmecophaga tridactyla* in the El Golfo local fauna is the first record of this species in North America, and extends the known northern range more than 3000 km (Fig. 3).

This record of *Myrmecophaga* represents the tenth family of South American origin that entered North America after the appearance of the Panamanian land bridge. Other South American groups that migrated northward during the late Pliocene and early Pleistocene include two families of caviomorph rodents (genera *Hydrochoerus, Neochoerus*, and *Coendou*), one didelphid marsupial (*Didelphis*), a vampire bat (*Desmodus*) (*9*), and five families of xenarthrans including ground sloths (*Glossotherium* and *Nothrotheriops*), armadillos (*Dasypus* and *Holmesina*) and glyptodonts (*Glyptotherium*).

Previous studies of this Great American Faunal Interchange (*10, 11*) between North and South America considered *Myrmecophaga tridactyla* as a strictly tropical form. As such, it was not included in calculations of faunal diversity and equilibrium for the temperate portion of the North American fauna.

Webb and Marshall (*12*) recognize three phases (*13*) to the Great American Faunal Interchange, with the third phase subdivided into two parts. Phase 3B in the North American Irvingtonian record is defined by the first appearance of the following South American genera: *Didelphis, Desmodus, Eremotherium, Nothrotheriops, Erethizon*, and *Hydrochoerus*. *Hydrochoerus, Didelphis*, and *Eremotherium* are restricted to the Gulf Coast and Florida and cannot be considered in the context of the El Golfo local fauna. *Desmodus* is predominantly southeastern in distribution, with only one late Pleistocene record in western North America. White (*14*) considers *Erethizon* (not present in the El Golfo local fauna) to be an autochthonous genus derived from *Coendou*. Of these genera, only *Nothrotheriops* occurs at El Golfo.

We now add *Myrmecophaga* to the phase 3B cohort of the interchange. Evidently it entered North America during Irvingtonian time when more tropical conditions prevailed (*15*). The presence of *Geochelone* sp. (*16*), *Constrictor constrictor* (*17*), *Neochoerus* sp., *Cuvieronius* sp., and *Tapirus* sp., along with *Myrmecophaga*, further indicates that the climate at El Golfo was more tropical during that part of the early Pleistocene. Today, the Sonoran Desert of Arizona, California, and adjacent Mexico is a subtropical, warm desert that rarely experiences sustained freezing temperatures (*18*). Absence of these genera may be attributed to changes in rainfall and vegetation rather than temperature.

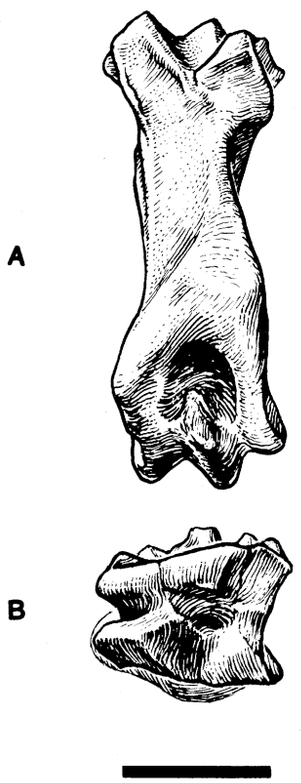

Fig. 2. Dorsal (**A**) and proximal (**B**) view of SDSNH 20323, the right metacarpal III of the giant anteater, *Myrmecophaga tridactyla*, from the Irvingtonian of Sonora, Mexico. Scale bar, 2 cm. [Illustration by Mark Hallett]

Fig. 3. Modern geographic range of the giant anteater, *Myrmecophaga tridactyla* (diagonal lines) [after Wetzel (*8*)]. The occurrence of this species in northwestern Sonora, Mexico (black circle), represents a Pleistocene range extension of over 3000 km. Stars indicate other Pleistocene records of this species.

Addition of *Myrmecophaga tridactyla* to the mammalian fauna that took part in the Great American Faunal Interchange helps define the environment at the isthmus and along the adjoining dispersal corridor. Previous evidence indicated that, unlike today, the isthmian region was predominantly savanna and that its climate was subhumid, presenting an array of mesic to seasonally arid habitats (*11, 12*). Presently, El Golfo is located on the edge of a Sonoran creosotebush scrub desert (*18*), but it is clear that climatic conditions similar to those along the dispersal corridor also existed there in early Pleistocene times. However, by the late Pleistocene, areas within the Sonoran Desert changed to pinyon-juniper-oak woodland and fluctuations in the size of these woodlands were rainfall-dependent (*18*). The current desert climate and plant associations are a relatively recent phenomenon.

Today, *Myrmecophaga* has a tropical distribution and uses most terrestrial habitats within its range, from lowland rain forests, foothills, and moist savanna through deciduous forests and parklands to semiarid thorn scrub and steppe (*8*). It feeds predominantly on a rich supply of ants and termites for which it forages widely (*19*). Failure of extant anteaters to penetrate into temperate regions is attributed to the seasonality of food resources and their difficulty in maintaining a constant body temperature in a cooler environment without an appreciable

expenditure of energy (*20*). More specifically, they may be limited by the availability of abundant ant nests and termitaria. Presumably more equable climates and year-round availability of ants and termites existed at El Golfo in the early Pleistocene.

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Steroidogenesis-Activator Polypeptide Isolated from a Rat Leydig Cell Tumor

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A cycloheximide-sensitive protein responsive to adenosine 3′,5′-monophosphate has been postulated to participate in the regulation of cholesterol side-chain cleavage activity in steroidogenic tissues. Such a steroidogenesis activator polypeptide (SAP) had been isolated from rat adrenocortical tissue and partially characterized. Now a polypeptide with comparable chromatographic behavior and biological activity has been purified from the rat H-540 Leydig cell tumor in quantities sufficient for amino acid sequencing. The activator contains 30 amino acid residues and has a molecular weight of 3215. The synthetic construct based on this sequence is virtually equipotent with native H-540 tumor SAP in an adrenal mitochondrial cholesterol side-chain cleavage assay. Hormonal regulation of the intracellular concentration of this activator may control the rate of cholesterol metabolism in steroidogenic organs.

THE HORMONALLY REGULATED, committed reaction in steroid formation—the conversion of cholesterol to pregnenolone by the cholesterol side-chain cleavage (cholesterol scc) cytochrome P-450 complex (*1*)—is acutely sensitive to inhibitors of protein synthesis (*2, 3*). Considered with the rapid metabolic response of steroidogenic tissues to appropriate hormonal stimuli, this observation suggested the existence of a labile intracellular protein mediator of adrenocorticotropin (ACTH) and gonadotropin action on pregnenolone formation (*3, 4*) that is increased in activity by adenosine 3′,5′-monophosphate (cAMP) (*5, 6*).

A factor in the adrenal cortex of rats implanted with an ACTH-secreting tumor was identified (*7*) as a steroidogenesis activator polypeptide (SAP) that exhibits many of the characteristics imputed to the hypothetical modulator. However, the quantities of material available were inadequate for a successful determination of its primary structure. Therefore, we turned to the H-540 rat Leydig cell tumor as a source that might be enriched in the activator. This approach was suggested by two observations. First, a material that is chromatographically similar to adrenal SAP and that enhances cholesterol scc activity in the adrenocortical mitochondrial assay can be detected in the testis of the normal postpubertal rat (*8*). Second, the H-540 Leydig cell tumor contains substantial cholesterol scc activity that is responsive to gonadotropins or cAMP and sensitive to cycloheximide (*9*).

The isolation of H-540 tumor SAP was accomplished by minor modifications of the protocol described for adrenocortical SAP (*7*). Material eluting in a low molecular-weight range (1500 to 6000) during size-exclusion high-performance liquid chromatography (HPLC) was collected, neutralized, and subjected to reversed-phase HPLC (Figs. 1 and 2A). Chromatography fractions were monitored for stimulation of cholesterol scc activity (Fig. 1), and the material in the region of interest was rechromatographed twice to obtain a preparation (Fig. 2A) that was homogeneous by NH_2-terminal amino acid analysis (isoleucine) (*10*).

A comparison of adrenocortical SAP (*7*) and Leydig cell tumor SAP suggested that each has a dose-dependent effect on cholesterol scc activity when measured with either adrenocortical or H-540 tumor mitochondria (Table 1). In the adrenocortical assay system, $10^{-8}M$ or $10^{-7}M$ concentrations of each activator stimulated cholesterol conversion to about 1.5 or 6 times, respectively, the activity of control incubations. At the higher concentration of polypeptides, this increase is comparable to that observed in the adrenal mitochondria of stressed rats (*11*). With mitochondria from the Leydig cell tumor, the overall levels of enzyme activity were predictably (*9*) lower (Table 1), but both of the polypeptides produced effects qualitatively similar to those seen in the adrenocortical assay system.

From a tryptic digest of 4.4 nmol of H-540 SAP (25 tumors), three fragments were resolved by reversed-phase HPLC (Fig. 3) and sequenced manually by Edman degradation (*10*). The phenylthiohydantoin (PTH) amino acids were identified by reversed-phase HPLC. Vapor-phase microsequencing (*12*) of 0.8 nmol of intact H-540 tumor SAP, carried out through residue 28, was used to confirm these sequence data and to establish fragment order. The 3215-dalton

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