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Convergent and Alternative Designs in the Digital Adhesive Pads of Scincid Lizards

Abstract. Prasinohaema virens, *an arboreal scincid lizard, differs from its closest relatives in that it exhibits subdigital adhesive setae resembling those of anoles in shape and those of geckos in some aspects of size. The other scincid species in this genus as well as those in a presumed ancestral genus exhibit pad scales with surface folds and ruffles but no setae; at least one of these species uses an adhesive grip similar to that of anoles and geckos. Thus, there appear to be two strikingly different epidermal specializations for adhesive grip within this small radiation.*

Two primarily arboreal groups of lizards, the family Gekkonidae and the anoline section in the family Iguanidae, have subdigital pads covered with microscopic hairs or setae. Setae enable the animals to climb by adhering to surfaces that will not accept the claw, such as smooth walls, leaf surfaces, and glass. Geckos and anoles each constitute large, diverse radiations whose success is at least in part based on the adaptive value of the adhesive pad (*1, 2*). Several arboreal lizards in the family Scincidae have adhesive pads that are grossly similar to those of anoles and geckos, and previous descriptions of sectioned and whole digits suggest the presence of setae (*3, 4*). Scanning electron microscopy of these forms (*5*) reveals that one species, *Prasinohaema virens*, exhibits remarkable convergence in setal morphology to *Anolis* and some geckos, whereas the reputed closest relatives of *P. virens* exhibit a wholly different pad fine structure.

The setae of *Prasinohaema virens* and *Anolis* are similar in shape (Fig. 1, A, B, D, and E). There is a triangular tip attached at the apex to a tall unbranched stalk; but the *P. virens* setae are significantly larger and less densely packed than those of any anoline examined to date (*5*) (Table 1). The seta stalk diameter, the density of stalks, and the total tip area per stalk are more like those of some geckos, although the basic shape or design of the seta is distinct from that of most geckos (Table 1 and Fig. 1, A and B and F to H) (*1, 6*). The adhesive setae of some Coleoptera approach those of *P. virens* in size and shape (*7*).

Prasinohaema virens and the other scincid lizards that we examined are a terminal twig of the most evolutionarily derived of the four subfamilies of the

Table 1. Comparison of setal morphology.

Item	*Prasinohaema virens*	*Anolis cuvieri*	*Gekko gecko* (*6*) (*Gekko vittatus*)
Setal shape	Single stalk ending in a triangular tip	Single stalk ending in a triangular tip	Multibranched stalk ending in 100 to 1000 small triangular tips
Stalk dimensions			
Diameter (μm)	2.0 ± 0.2	0.51 ± 0.04	5 (2.1 ± 0.3)
Height (μm)	26.0 ± 2.0	22.4 ± 0.5	110 (33 to 42)
Stalk density (stalks per square micrometer)	0.03	1	0.005 (0.01)
Tip dimensions			
Length (μm)	6.2 ± 0.4	0.624 ± 0.045	0.2 (0.2)
Width (μm)	6.3 ± 0.4	0.729 ± 0.045	0.2 (0.2)
Estimated area (μm^2)	19.5 ± 1.7	0.229 ± 0.025	0.02
Estimated total tip area per stalk (μm^2)	19.5 ± 1.7	0.229 ± 0.025	2 to 20
Ratio of estimated total tip area to cross-sectional area of stalk	6.2	1.1	0.1 to 1.0

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Scincidae (*8*). They are, therefore, phyletically very remote from anoles (derived iguanids) (*9*) or the advanced geckos (primitive geckos lack pads) (*1*). The *P. virens* setae resemble anole setae in shape and gecko setae in some dimensions, but they represent a third, perhaps unique, design for setae in lizards.

The *P. virens* setae also appear to have an unusual morphological derivation. The setae of both anoles and geckos are believed to be derived from spinules or small spines that cover the surface of nonpad, generalized scales (*3, 6*). In *P. virens*, its relatives, and all the other scincids examined to date, the generalized digital scale surface does not exhibit spines or spinules (*3, 10*). The epidermal cell surface is smooth, and the cells are elongated normal to the long axis of the digit (Fig. 1I). Cell margins with toothlike edges form what has been termed the lamellate-dentate pattern (*3, 10*). Ostensibly, it is far more difficult for setae to evolve from a smooth lamellate-dentate surface than to evolve by enlargement and differentiation of spines. The *P. virens* morphology offers only one clue as to how the setae evolved. Near the margins of the field of setae the stalks are shorter and the triangular tip is poorly differentiated (Fig. 1C); the stalks appear to arise from (or in close association with) a reticular pattern of elevations. More peripherally on the pad scales and on the surface of scales adjacent to the pad these reticular elevations merge into the lamellate-dentate margins (Fig. 1J). The difference between the reticular and lamellate-dentate architecture is largely in the shape of the presumed epidermal cells; the area of the surface enclosed by the lamellate-dentate margins and the reticular elevations is not markedly different. Unlike the setae of geckos and anoles, the scincid setae may have arisen as elaborations of the epidermal cell boundaries.

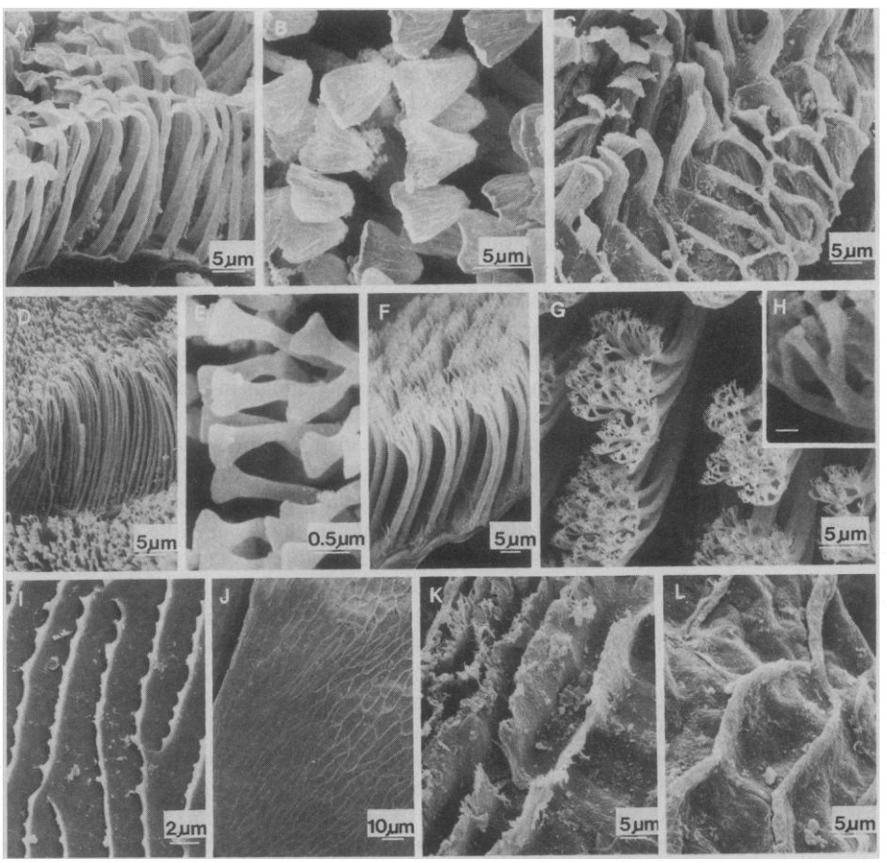

Fig. 1. The comparative morphology of setae and ruffles. (A) Lateral view of the setae stalks and tips in *Prasinohaema virens*. (B) Ventral view of the setae tips. (D and E) Comparable views of the setae in *Anolis cuvieri*. (F and G) Lateral and ventral views of the setae in *Gecko vittatus*. (H) Detail of (G) showing the seta tip [scale in (H), 0.25 μm]. The differences in size and shape are apparent by comparing the lateral views of the stalks. The skink (A) and anole (D) setae are shown at the same magnification. They are similar in shape but obviously differ in stalk diameter and density. The gecko setae (F) are branched, but the stalk diameter and density are similar to those of *P. virens*. Ventral views of the setae tips (B, E, G, and H) illustrate the similarity in triangular shape but marked variation in tip area. The anole (E) and skink (B) setae are shown at a similar size, but the dimensional scales reveal the order-of-magnitude difference in size. (C) Poorly differentiated setae along the lateral margin of a pad scale in *P. virens*. Setae stalks appear to arise from reticular elevations of the epidermal cell boundaries. (I) Lamellate-dentate architecture of a generalized, nonpad scale adjacent to the claw; the cells are elongated normal to the long axis of the toe, and the margins have small toothlike extensions. (J) Scale just distal to the pad in *P. virens* where reticular architecture (upper right), similar to that shown in (C), grades into the lamellate-dentate pattern (lower left), similar to that shown in (I). (K) Ruffled scale surface of *Lipinia longiceps*; the area shown is toward the proximal (rear) portion of the scale. (L) Reticular pattern of low folds lying along the distal margin of the scale in *L. noctua*. Exaggeration of the dominant, transversely oriented folds (shown running from top right to lower left) could produce transversely oriented folds and ruffles similar to those in (K). The reticular-like arrangement of the low folds in (L) suggests that the setae of *P. virens* and the fold-ruffle design of its relatives may be linked to the primitive lamellate-dentate scale architecture through a specialized reticular arrangement of the epidermal cells. In (A), (B), (D to F), and (L) the distal end of the toe and the claw are toward the right. In (C) the claw is toward the top right. In (G) and (H) the claw is toward the bottom, and in (I to K) the claw is toward the left.

The genus *Prasinohaema* includes three species of Papuan and Solomon Islands skinks that have green pigment in the blood plasma (*8*); *P. virens* is, in some ways, the most primitive species assigned to the genus and has obvious similarities in habitus and color pattern to *Lipinia*, a presumably ancestral genus of slender arboreal skinks (*8*). *Prasinohaema flavipes, P. prehensicauda, Lipinia noctua, L. leptosoma*, and *L. longiceps* have a subdigital pad, but there is no evidence of setae. The surface of the pad scales is raised into folds (elevation 2 to 10 μm), which often have frayed borders like ruffles (Fig. 1K). A series of parallel ruffles on each scale are arranged normal to the long axis of the digit. The evolutionary and developmental relationships between the ruffles and folds and the lamellate-dentate surface are much clearer than those between setae and the lamellate-dentate surface. However, the ruffles are probably not simple elevations of a single lamellate-dentate margin. The area of the ruffles plus that between adjacent ruffles is much greater than the area bounded by lamellate-dentate margins, and what appear to be cell junctions occur on the surface of the ruffles in some places. The region of the scale proximal and lateral to the ruffles often has a reticular pattern of low folds similar to the reticular surface adjacent to the setae of *P. virens*, except that the reticular boundaries have dominant transverse and longitudinal orientations (Fig. 1L). The distance between the transverse reticulae is similar

to the distance between the ruffles and folds. Exaggeration of the transverse reticulae formed by the boundaries of a series of cells could produce the folds and ruffles. The morphology of the scale surfaces suggests that the setae of *P. virens* and the fold-ruffle design found in related species are alternative specializations of a reticular arrangement of cell boundaries, which is itself derived from the primitive lamellate-dentate pattern.

The behavior of the scincid species we examined is poorly known. The original description of *Lipinia (Aulacoplax) leptosoma* (*4*) indicates that *L. leptosoma* leap 1½ to 2 feet or more between leaf surfaces and climb vertical and overhanging glass surfaces. In behavioral terms, the ruffle-fold architecture appears to be functionally comparable to setae—it can establish a grip that supports the animal. This makes the divergence of *P. virens* even more problematical, for if a ruffled scale surface can establish an "adhesive" grip as do setae, and the fold-ruffle architecture exists in the more primitive members of the radiation, the adaptive significance of the shift to setae in *P. virens* is unclear.

Among lizards, at least four different fine structural designs are capable of forming an adhesive grip—three types of setae (*6*) and the fold-ruffle morphology. It is not yet possible to interpret the functional significance of the differences among the setae nor those between the setae and ruffles, but the morphological comparisons reveal a variety of interesting evolutionary patterns. Convergence in setal morphology and alternative designs for adhesion in distantly related lineages, such as anoles and the scincid species other than *P. virens*, are examples of relatively common themes in comparative morphology. Striking divergence of closely related species and the appearance of a complex specialization as an isolated species [or generic (*11*)] adaptation is less common. The *P. virens* fine structure appears to illustrate very rapid morphological change relative to the taxonomic rate of evolution. Investigation of the adaptive significance of cases such as this—illustrating striking morphological divergence at low taxonomic levels—may provide insight into the evolution of new adaptive complexes.

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11. The presence of setae in *P. virens* might indicate that it is a member of a lineage separate from *P. flavipes* and *P. prehensicauda*. If this is true it cannot be retained in *Prasinohaema* (type *flavipes*). A new genus for *virens* may be required.
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Tumor Imaging with Radioactive Metal Chelates Conjugated to Monoclonal Antibodies

Abstract. *High-resolution gamma camera images of mouse erythroid tumors were obtained by use of leukemia cell–specific monoclonal antibodies labeled with bifunctional radioactive metal chelates. Small tumors (200 to 300 milligrams) were visible without subtraction or enhancement 1 to 5 hours after injection of antibody. Chelate-derivitized monoclonal antibodies permit targeting of a broad spectrum of radioisotopes, including those that are optimum for gamma camera imaging or positron tomography, as well as those that are tumoricidal.*

Imaging of tumor-specific antibodies labeled with radioactive isotopes has the potential to be a relatively noninvasive, yet sensitive, diagnostic procedure for visualizing otherwise undetectable tumors and metastases (*1*). In addition, the labeled tumor-specific antibodies may have tumoricidal effects (*2*). Development of techniques for preparing monoclonal antibodies (*3*), some with absolute tumor specificity (*4*), has encouraged such an approach. Although experimental tumor imaging, as well as therapy with radioactively labeled antibodies, has usually been done with immunoglobulins labeled with iodine isotopes (*1*), the iodine isotopes are not ideal for scanning. Of the three commonly available isotopic forms, only iodine-123 has the appropriate emission characteristics for imaging and a short enough half-life to be safely used diagnostically. The gamma radiation of iodine-125 is too weak for imaging. Iodine-131 has often been used (*1*), but is undesirable because of its long half-life and high-energy gamma and cytotoxic beta radiations. Iodine-131 has also been used therapeutically for large tumors (*2*), but appears ineffective in the treatment of small tumor foci or metastases (*5, 6*). Furthermore, the rapid metabolism of specifically bound radioiodinated antibodies leads to the incorporation of metabolized iodine into the thyroid and the active excretion of iodine by the stomach and urinary tract, preventing specific tumor imaging (*6, 6a*).

A more versatile method for labeling of antibodies is the use of covalently attached bifunctional radiometal chelates (*5, 7*). Chelatable radioactive metals with half-lives ranging from 1 hour to 3 days are available (*8*). Of these, gallium-67, indium-111, and technetium-99m are optimum for gamma camera imaging; gallium-68 is optimum for positron emission tomography; and scandium-47 or alpha-emitting isotopes are optimum for therapeutic effects. Khaw *et al.* (*7*) demonstrated the utility of this method with ^{111}In-labeled diethylenetriaminepentaacetic acid (DTPA) conjugated to rabbit antibodies to canine cardiac myosin Fab fragments for imaging myocardial infarcts in dogs.

We have used Rauscher murine erythroleukemia as a model system for studies of the diagnostic and therapeutic potential of monoclonal antibodies (*5, 6*). This disease, induced by the Rauscher

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