Attachment of Vimentin Filaments to Desmosomal Plaques in Human Meningiomal Cells and Arachnoidal Tissue

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ABSTRACT Desmosomal proteins are co-expressed with intermediate-sized filaments (IF) of the cytokeratin type in epithelial cells, and these IF are firmly attached to the desmosomal plaque. In meningiomal and certain arachnoidal cells, however, vimentin IF are attached to desmosomal plaques. Meningiomas obtained after surgery, arachnoid "membranes," and arachnoid granulations at autopsy, as well as meningiomal cells grown in short-term culture have been examined by single and double immunofluorescence and immunoelectron microscopy using antibodies to desmoplakins, vimentin, cytokeratins, glial filament protein, neurofilament protein, and procollagen. In addition, two-dimensional gel electrophoresis of the cytoskeletal proteins has been performed. Using all of these techniques, vimentin was the only IF protein that was detected in significant amounts. The junctions morphologically resembling desmosomes of epithelial cells have been identified as true desmosomes by antibodies specific for desmoplakins and they provided the membrane attachment sites for the vimentin IF. These findings show that anchorage of IF to the cell surface at desmosomal plaques is not restricted to cytokeratin IF as in epithelial cells and desmin IF as in cardiac myocytes, suggesting that binding to desmosomes and hemidesmosomes is a more common feature of IF organization. The co-expression of desmosomal proteins and IF of the vimentin type only defines a new class of cell ("desmofibrocyte") and may also provide an important histodiagnostic criterion.

Among the intercellular junctions, desmosomes (maculae adhaerentes) have distinctive morphological (10, 13, 47, 67) and biochemical (4, 6, 25, 28, 33, 39, 53) criteria. The typical multilayer organization of desmosomes is characterized by an extracellular midline (*stratum centrale*), the two plasma membrane domains, and the two plaques at which usually bundles of cytoplasmic intermediate-sized filaments (IF)[1] anchor. Analysis of the protein composition of desmosomal fractions from bovine muzzle epidermis has revealed six major polypeptides ranging from M_r 250,000 to 75,000 (4, 6, 25, 53, 62). Among the diverse intercellular connections such as tight junctions (zonula occludens), gap junctions (nexus), and intermediate junctions (zonulae and fasciae adhaerentes, puncta adhaerentia) desmosomes are typical features of epithelial cells. Using antibodies to different IF and antibodies to desmoplakins, the major constitutive polypeptides of the desmosomal plaque (M_r 250,000 and 215,000), it could be shown that filaments of the cytokeratin type are specifically attached to the desmosomal plaques in epithelial cells (25, 28, 33). Therefore, the presence of desmosomal proteins and cytokeratins in the same cell can be taken as a biochemical marker for epithelial tissues and tumors derived therefrom (28, 29). However, in cardiac myocytes that do not contain cytokeratins but are connected by desmosomal structures containing similar proteins as epithelial desmosomes (28, 46), the IF attached to the desmosomal plaques have been identified as desmin filaments (46, 72).

From immunofluorescence studies of a broad diversity of human tumors we have noted that desmoplakins also occur in one cell type that expresses neither cytokeratin nor desmin

[1] *Abbreviations used in this paper:* IF, intermediate-sized filaments.

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IF but only IF of the vimentin type. These are meningiomas, i.e., intracranial tumors believed to be derived either from arachnoidal cells or, from arachnoid granulations, and that are known to contain junctions with a desmosome-like morphology (3, 5, 41, 54, 59, 70). In the present study we show that these junctions indeed contain typical desmosomal proteins and that in these cells vimentin IF are attached to the desmosomal plaques. The results demonstrate that attachment of filaments to desmosomal plaque structures is not restricted to filaments of the cytokeratin and desmin types but also extends to vimentin IF, suggesting that the interaction with desmosomal plaque protein is also a characteristic of vimentin IF proteins.

MATERIALS AND METHODS

Tissues and Cells: Human meningiomas were obtained during surgical removal and processed for electron or light microscope preparation within 30 min. Arachnoid "membranes" and arachnoid granulations were taken from human corpses ~8–24 h post mortem and either directly frozen or fixed with aldehydes. For preparation of cultures of human meningioma cells, the tissue was cut into small pieces, washed with PBS, incubated several times in trypsin solution, and stirred for 5 to 15 min. Cells dissociated from the tissue were collected after each incubation step by centrifugation at 500 *g* for 5 min. Such preparations enriched in isolated cells were washed twice with culture medium (Dulbecco's modified Eagle's medium). The cells were grown in Petri dishes for several passages (for details see reference 15). For microscopic studies, cells grown in passage 2, 3, or 4 were used.

Preparation of Cytoskeletons and Microdissection: Preparations of cytoskeletal material were made from frozen arachnoid membranes and arachnoid granulations following procedures described for other tissues (19, 23, 50, 51). Cytoskeletal material from meningiomas was prepared by microdissection from cryostat sections (ca. 20 μm thick) after transfer to microscope slides and air-drying. Care was taken to remove stromal tissue and blood vessels as far as possible, using a fine needle (for details see references 51 and 52). The samples were transferred to centrifuge tubes and extracted with high salt buffer and Triton X-100 as described (51, 52). For two-dimensional gel electrophoresis we routinely applied the equivalent of 0.25-cm^2 tumor areas microdissected from 10–15 sections.

Antibodies: The following antibodies were used: (*a*) guinea pig antibodies to desmoplakins from bovine muzzle (28, 53); (*b*) guinea pig antibodies to murine and human vimentin (23); (*c*) affinity-purified sheep antibodies to vimentin (a generous gift from Dr. M. Osborn, Max-Planck-Institute for Biophysical Chemistry, Goettingen, Federal Republic of Germany); (*d*) guinea pig antibodies to bovine epidermal prekeratins purified by preparative gel electrophoresis (24); (*e*) murine monoclonal antibody (K_G 8.13) with a broad range of cross-reactivity between the "basic subfamily" (64) of cytokeratins polypeptides (36); (*f*) guinea pig antibodies to desmin from chicken gizzard that cross-reacted with mammalian desmin (46, 65); (*g*) rabbit antibodies to desmin from human uterus (31); (*h*) affinity-purified rabbit antibodies against the M_r 68,000 polypeptide of neurofilaments from rat brain ([61]; generously provided by M. Osborn); (*i*) mouse monoclonal antibodies to the 200,000 polypeptide of neurofilament ([8]; generously provided by M. Osborn); (*j*) rabbit antibodies to glial filament protein from pig spinal cord ([56, 60]; generously provided by M. Osborn); (*k*) rabbit antibodies to glial filament protein (generously provided by Dr. A. Bignami and Dr. D. Dahl, Dept. of Neuropathology, Harvard Medical School, Boston, MA); (*l*) rabbit antibodies to precollagen type I (generously provided by Dr. Timpl, Max-Planck-Institute for Biochemistry, München, Federal Republic of Germany).

Microscopy: Indirect immunofluorescence microscopy of 4-μm cryostat sections, acetone-fixed at −20°C for 10 min, was performed as described (25). Cultured meningioma cells grown on coverslips were processed for immunofluorescence microscopy after fixation in methanol (−20°C, 10 min) and acetone (−20°C, 15 s) as described (25). For double immunofluorescence microscopy first antibodies were applied simultaneously. As second antibodies, we used rhodamine-labeled goat antibodies against guinea pig and mouse IgG, and fluorescein-labeled goat antibodies against guinea pig IgG and rabbit antibodies against sheep IgG. For immunolocalization at the electron microscopic level, cryostat sections were fixed for 10 min in acetone (−20°C) and incubated with guinea pig antibodies to desmoplakins or vimentin for 40 min. Sections were washed three times with PBS for 15 min and incubated with goat IgG (1 μg/ml) for 20 min, prior to incubation (16 h, room temperature) with goat IgG against guinea pig IgG that had been coupled with colloidal gold particles (5-nm diam; Janssen Pharmaceutics, Beerse, Belgium). After repeated washing with PBS, sections were fixed in 2.5% glutaraldehyde (30 min, 50 mM cacodylate buffer, pH 7.2) and 2% OsO_4 (30 min, same buffer), and processed for thin sectioning. For electron microscopy of ultrathin sections tissues and cells grown on coverslips were fixed, dehydrated, embedded, and sectioned as described (17–19).

Gel Electrophoresis: One-dimensional gel electrophoresis using 8% slab gels was performed according to Laemmli (49). For two-dimensional gel electrophoresis isoelectric focusing or nonequilibrium pH gradient electrophoresis were applied (ampholine range pH 2–11) for separation in the first dimension according to O'Farrell and colleagues (55).

RESULTS

Meningiomas

Histological and electron microscopic characterizations of the two main classes of meningiomas, i.e., endotheliomatous and fibroblastic meningiomas, have been presented by previous authors (for literature see reference 48). In the present study, immunofluorescence and immunoelectron microscopy were applied to cryostat sections using antibodies to different intermediate filament proteins and desmoplakins, the major proteins of the desmosomal plaque of epithelial and myocardial cells (28, 29, 46, 53). Antibodies to vimentin were strongly positive on all meningiomal cells (Fig. 1, *a* and *c*) and decorated fibrillar structures extending throughout the cytoplasm. Double immunofluorescence microscopy using antibodies to vimentin and precollagen type I revealed that the vimentin positive cells were also positive with the procollagen antibodies. By contrast, antibodies to cytokeratins, desmin, glial filament protein, and neurofilament proteins in all cases gave negative results (not shown). Punctate fluorescence, in locally varying densities, was seen after staining with antibodies to desmoplakins (Fig. 1, *b* and *d*), especially along cell boundaries. On the basis of immunolocalization at the electron microscopic level in these (see below) and in epithelial cells (28, 29, 53), we interpret the individual fluorescent dots as the visualization of individual desmosomes or hemidesmosomes.

Although morphological differences between different subtypes of meningiomas are known (48), electron microscopic studies in general revealed a characteristic multilayer organization with long and often parallel cytoplasmic cell processes (Fig. 2*a*). Intercellular spaces varied in width and in some regions contained amorphous, densely stained material and masses of collagen fibers. Filaments of the intermediate type (7–11 nm) were abundant in all meningiomas. In some places the IF were distributed loosely and seemingly at random, in other areas they were arranged in loose-packed bundles as they have been described in the literature for vimentin filament bundles in other cell types (1, 23, 27, 38, 40, 44). Structures morphologically identical to desmosomes of epithelial cells were found in all meningiomas, revealing a prominent dotted midline, dense plaques on both cytoplasmic sides of the plasma membrane, and plaque-associated IF (Fig. 2, *b* and *c*). The bundles of these filaments associated with the desmosomal plaques were not as densely fasciated as normally found in tonofibrils of epithelial cells.

Electron microscopic immunolocalization of desmoplakins, using gold-coupled second antibodies, showed specific reaction with the desmosomal plaques (Fig. 2*d*). Vimentin examined with the same technique showed antibody-gold particles on all IF bundles running throughout the cytoplasm, including those associated with the desmosomal plaques (Fig. 2, *e* and *f*). No staining was observed when antibodies to

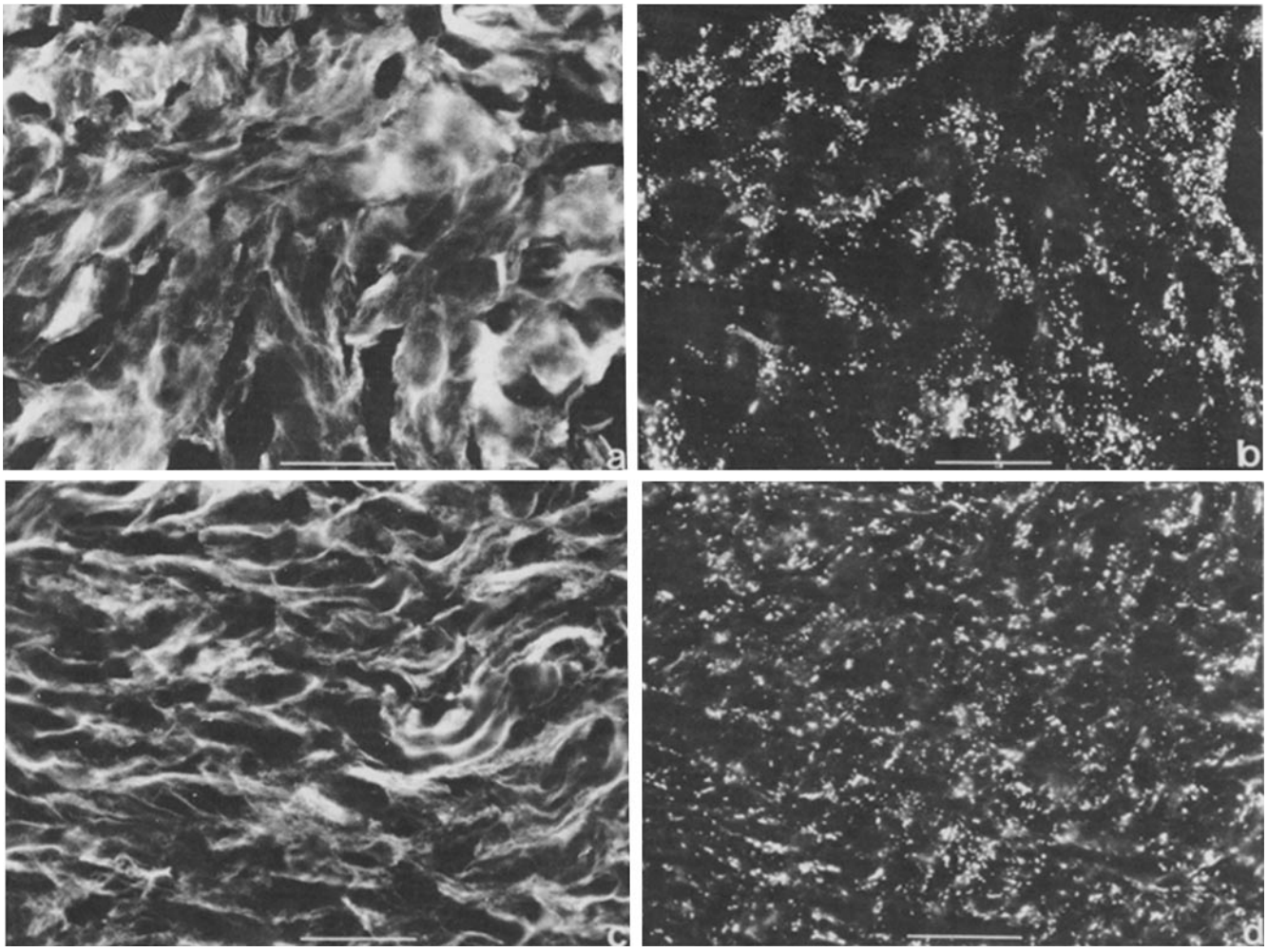

FIGURE 1 Immunofluorescence microscopy of cryostat sections of human meningiomas using antibodies to vimentin (*a* and *c*) and to desmoplakin (*b* and *d*). In *a* and *b* an example of the "endotheliomatous" tumor type is shown; in *c* and *d* the "fibroblastic" tumor type is shown. The dark nonfluorescent areas in both tumors represent extracellular spaces containing matrix material. Bars, 20 μm. × 820.

cytokeratins or desmin were applied in the same manner.

Cytoskeletal material of meningiomal cells obtained after microdissection from cryostat sections (ca. 20 μm thick) and extraction in high salt buffer and Triton X-100 from different meningiomas was examined by two-dimensional gel electrophoresis (Fig. 7*a*). Such preparations showed prominent enrichment of one polypeptide with the characteristic electrophoretic mobility of authentic vimentin, as demonstrable by co-electrophoresis of authentic vimentin from ^{35}S-labeled SV40-transformed human fibroblasts (SV80 fibroblasts, data not shown). No other IF proteins could be detected (for characteristic gel electrophoretic coordinates see references 2, 7, 26, 30, 50).

Arachnoidal Tissues

Arachnoidal "membranes" are composed of two cell layers, an "upper layer" facing the *dura mater*, which is built by almost isodiametric cells, and an "inner layer" facing the *pia mater*, which contains cells that are more irregularly-shaped, with long cytoplasmic projections, and contribute to the trabeculae spanning the subarachnoidal space. Interspersed between the cells of the inner layer are bundles of collagen fibers and small blood vessels. Arachnoidal granulations show, in addition, in some places infoldings of the "upper layer" and formation of local dense cell aggregates.

Immunofluorescence microscopy showed, on both cell layers, positive staining with antibodies to vimentin and desmoplakins (Fig. 3, *a–d*). Vimentin-positive cells were also positive for desmoplakins as demonstrated by double immunofluorescence microscopy, except for cells of blood vessels, which did not stain with desmoplakin antibodies. Antibodies to prekeratins, desmin, glial filament protein, and neurofilament proteins were negative.

Electron microscopy revealed a structural composition comparable with that of meningiomas (Fig. 4*a*). All cells contained abundant IF with undulating contours as well as desmosomes (Fig., *a* and *b*) and, occasionally, hemidesmosomes (Fig. 4*c*). Frequently, the desmosomes were very close to each other (Fig. 4*a*) and occupied a considerable proportion of the plasma membrane.

The desmosomal plaques showed lateral attachment with bundles of loosely packed IF (Fig. 4, *a–c*), which in some cases were also associated with surfaces of mitochondria (e.g., Fig. 4*a*). On two-dimensional gel electrophoresis of cytoskeletal proteins from both arachnoidal tissues vimentin was the only IF component identified (Fig. 7*b*).

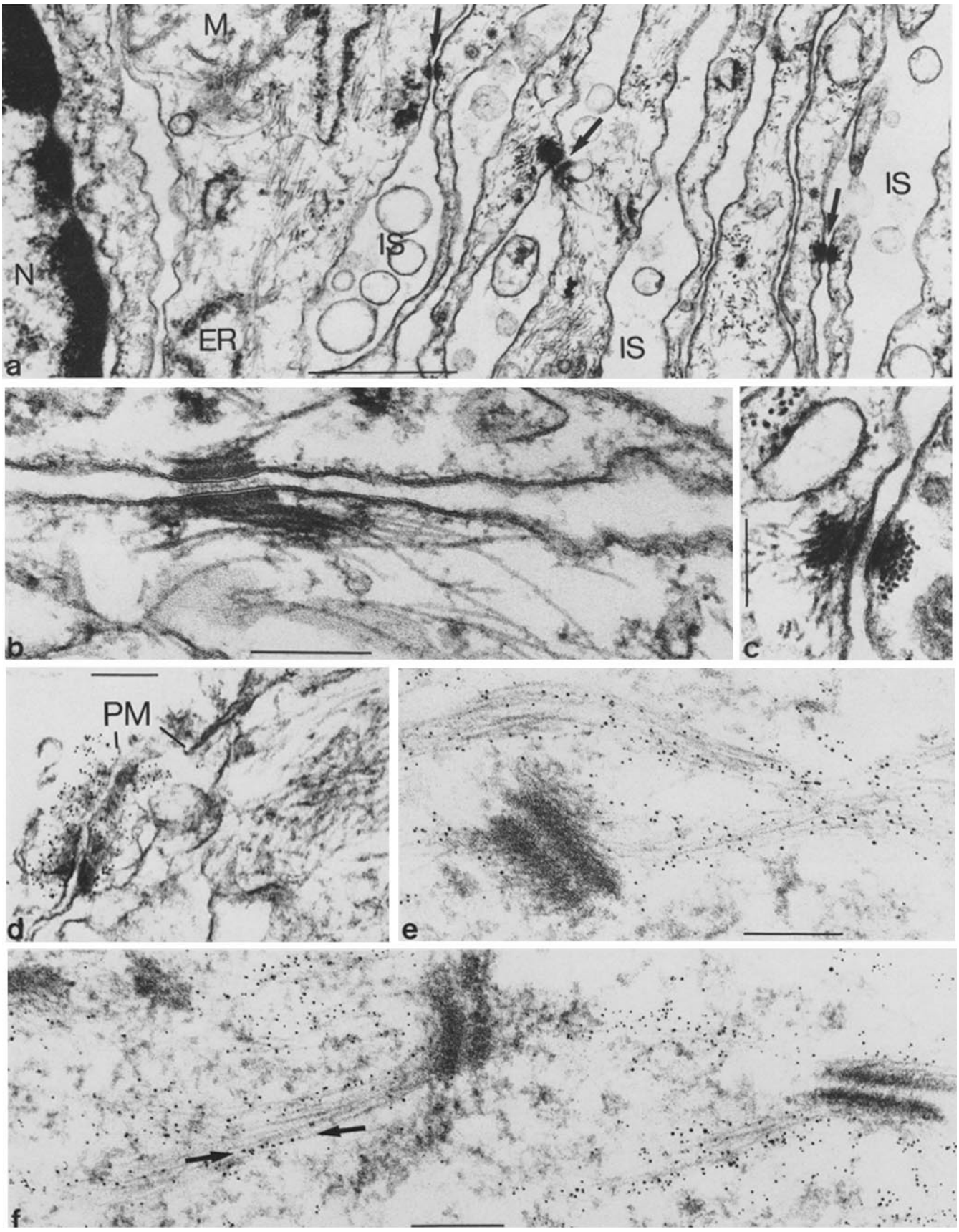

FIGURE 2 Electron micrographs of thin sections through meningiomas (*a–c*). (*a*) Survey picture showing numerous parallel cell processes that are rich in IF, mainly seen in cross section. Intercellular spaces (*IS*) are frequently interrupted by junctions resembling epithelial desmosomes (arrows). *ER*, endoplasmic reticulum; *M*, mitochondrium; *N*, nucleus. At higher magnification the typical morphological organization of the desmosomes is revealed (*b* and c). Longitudinally (*b*) and cross-sectioned (*c*) IF are

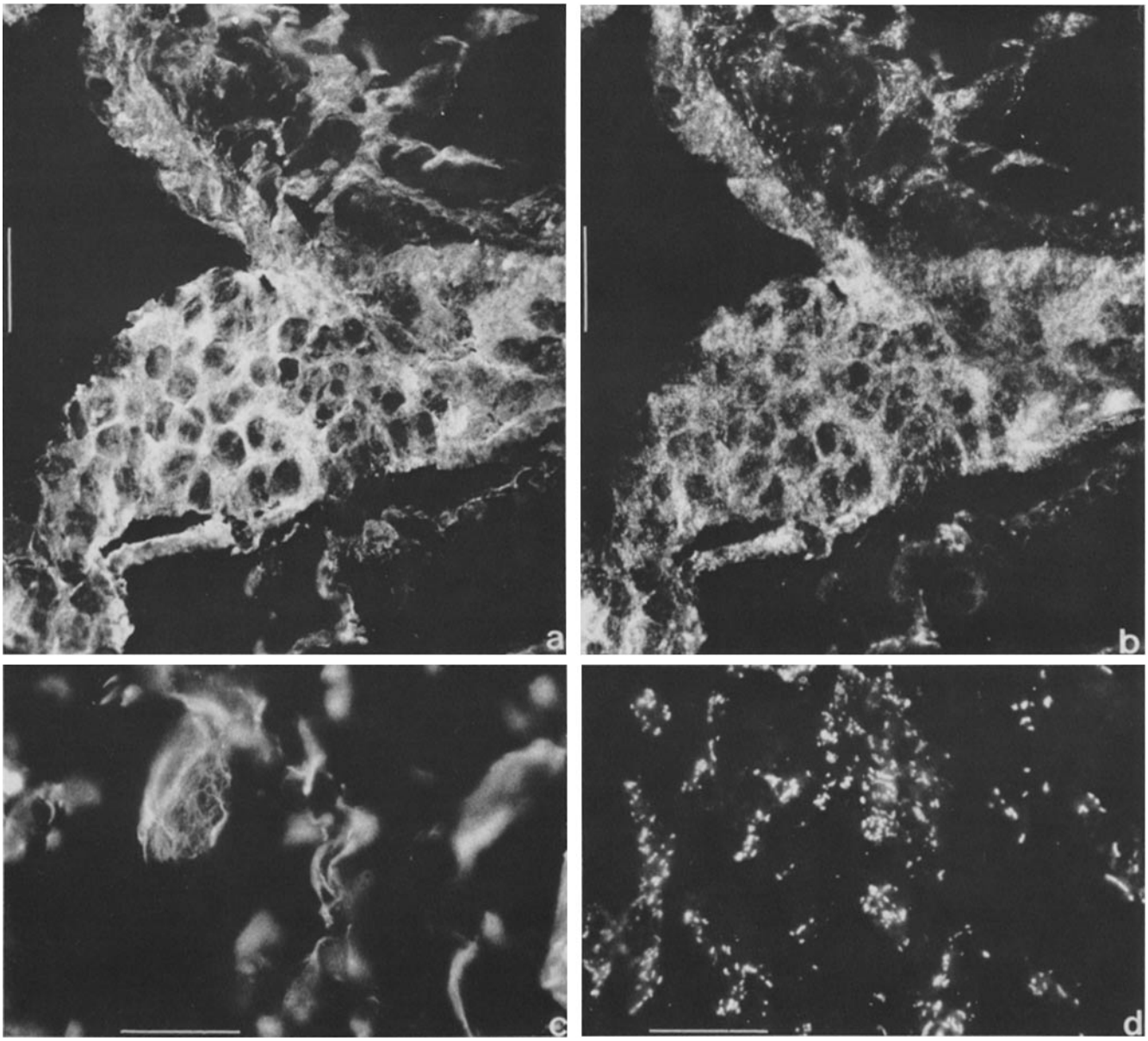

FIGURE 3 Double- (*a* and *b*) and single- (*c* and *d*) immunofluorescence microscopy of cryostat sections through arachnoidal granulations (*a* and *b*) and normal arachnoidal tissue (*c* and *d*). Incubation was performed with sheep antibodies to vimentin (*a*) mixed with guinea pig antibodies to desmoplakins (*b*), or after incubation with guinea pig antibodies to vimentin (*c*) or desmoplakin (*d*). Sheep antibodies were visualized by fluorescein isothiocyanate coupled second antibodies (*a*), and for staining of guinea pig antibodies rhodamine- (*b*) or fluorescein isothiocyanate-coupled (*c* and *d*) second antibodies were used. Both arachnoidal tissues show strong positive staining with vimentin (*a* and *c*) and desmoplakins (*b* and *d*). Vimentin-positive arachnoidal cells were also decorated by desmoplakins as seen by double immunofluorescence (*a* and *b*). The arachnoidal tissues usually show a composition of two distinct cellular layers: an upper layer formed by isohedral cells (cap cells, lining cells) that maintain prominent nuclei (central parts in *a* and *b*), and an inner layer of somewhat elongated cells with ellipsoidal nuclei and large intercellular spaces with stromal tissue (upper and lower part in *a* and *b*; *c* and *d*). Both cellular layers display comparably positive reaction with the antibodies to vimentin and desmoplakins. Bars, 20 μm. (*a* and *b*) × 790; (*c* and *d*) × 880.

laterally attached to the desmosomal plaques. These desmosome-attached IF appear as smoothly curved bundles of relatively loosely packed filaments. Immunoelectron microscopy using frozen sections of meningiomas after binding of antibodies to desmoplakins (*d*) and to vimentin (*e* and *f*), visualized by a second antibody coupled with 5 nm gold particles. The desmoplakin label strongly decorates the desmosomal plaques (*d*). All IF bundles are intensely labeled with gold including those anchored to desmosomal plaques (*e* and *f*). Sometimes the gold particles can be seen directly aligned on the individual filaments (arrows in *f*). Note absence of decoration on other cytoplasmic structures (*d–f*). *PM*, plasma membrane. Bars, 0.5 μm; 0.2 μm (*b–f*). (*a*) × 20,000; (*b*) × 125,000; (*c* and *f*) × 85,000; (*d*) × 60,000; (*e*) × 90,000.

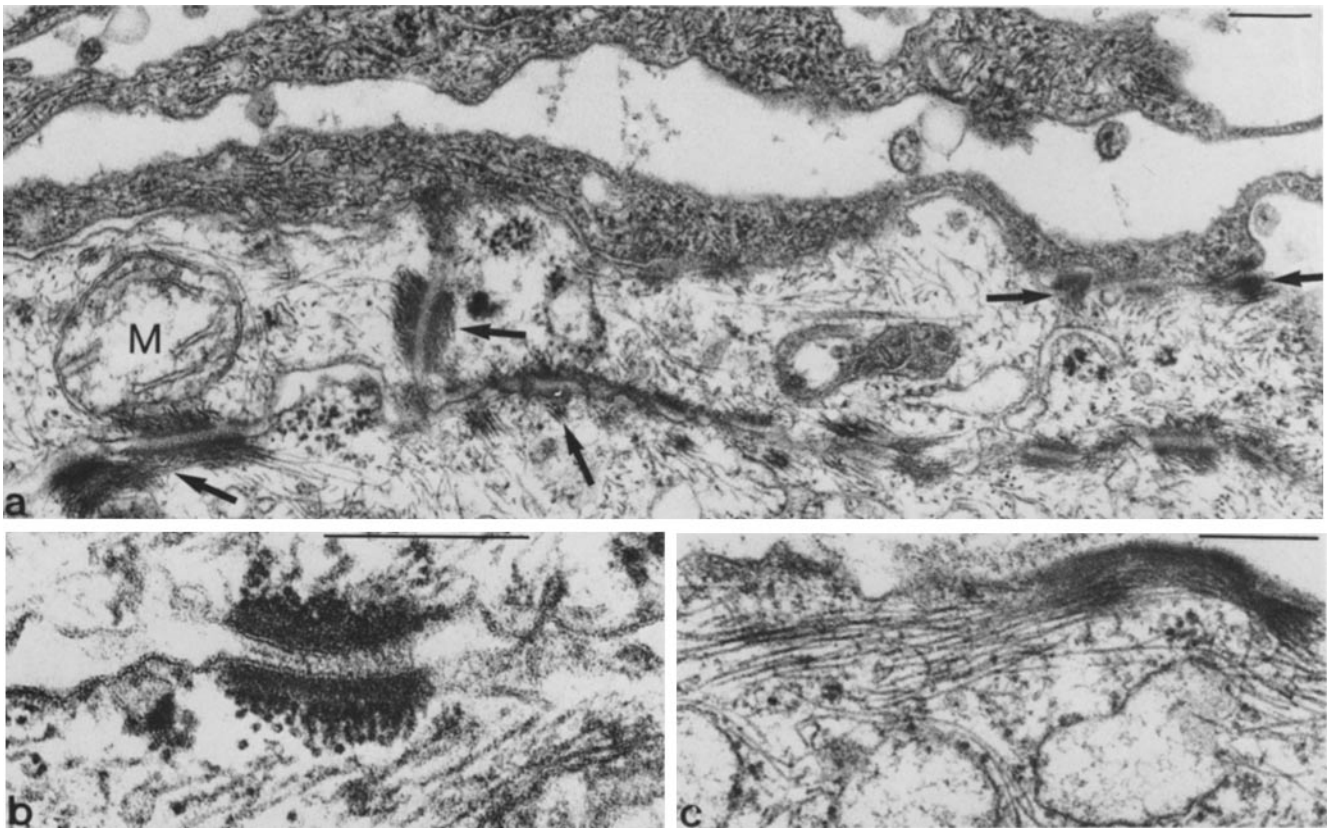

FIGURE 4 Electron micrographs of arachnoidal granulations (*a* and *b*) and normal arachnoidal "membranes" (*c*). The survey picture (*a*) shows the typical multilayer organization of arachnoidal granulations, with numerous desmosomes (indicated by arrows), and several small cellular projections, often separated by somewhat inflated intercellular spaces. Sometimes, IF anchored to desmosomal plaques are associated with mitochondria (*a*, *M*). In *c*, a hemidesmosome with a prominent desmosomal plaque and with associated IF is seen. Most of these IF appear in loose bundle arrays. Desmosome-attached IF in arachnoidal "membranes" exhibit in longitudinal (*a* and *c*) and cross sections (*b*) typical of IF organizations, identical to those of the desmosomes of meningiomas and arachnoidal granulations. Bars, 0.3 μm. (*a*) × 36,000; (*b*) × 90,000; (*c*) × 56,000.

Meningioma Cells in Culture

Human meningioma cells grown in short-term culture appeared as large flat cells with ovoid nuclei and numerous cytoplasmic processes that formed intercellular contacts. Immunofluorescence microscopy with antibodies to vimentin showed a characteristic decoration in these cells (Fig. 5*a*). Often, thick bundles of IF surrounded the nuclei and/or extended into the long cellular processes. Such massive IF arrays could also be detected by phase-contrast microscopy (Fig. 5*b*). In addition, thinner vimentin fibrils were noted which projected into the cell periphery (arrows in Fig. 5*a*). Dense monolayers grown for more than 6 d and stained with antibodies to desmoplakins displayed the typical appearance of fluorescent dots aligned at cell-to-cell boundaries (Fig. 5*c*). Most of these dots represented desmosomes or hemidesmosomes at the cell bottom but dots seemingly situated deeper in the cytoplasm (arrows in Fig. 5*c*) were also recognized at variable frequencies and were interpreted to represent internalized desmosomal structures (cf. 45, 46, 57).

Various antibody preparations to cytokeratins and desmin were used on these cultured meningioma cells and gave negative results. Only occasionally a few individual cells showed reaction with some of the cytokeratin antibodies but not with others, and this might indicate the existence of a small subclass of different cells present in these cultures (not shown). Using immunoelectron microscopy we found that, as in other cells (see above, and references 28, 29, 45, 46, 53, 66), desmoplakin antibodies localized at the desmosomal plaques (not shown) and that antibodies to vimentin decorated all IF in the cells examined, including those associated with the desmosomal plaques (Fig. 5, *d* and *e*).

In contrast to the above described meningiomas and arachnoidal tissue, the cultured meningioma cells could be fixed as living cells, thus allowing optimal preservation of cellular structures. IF were abundant and appeared in bundles or as single undulating fibrils. Cross sections revealed the hollow core organization of these filaments and inter-IF distances of 10–20 μm (Fig. 6*a*), which is typically observed in parallel arrays of filaments of the vimentin type (27). Desmosomes with laterally attached bundles of IF were frequently observed in dense cell cultures (Fig. 6*b*). In addition, a certain class of cytoplasmic vesicles associated with dense plaque material and IF bundles (Fig. 6*c*) could be identified which appeared either as disk-like symmetrical arrays, with normal-looking plaques and a well discerned midline (Fig. 6*c*), or as rounded-off vesicles with small residual plaque structures. These vesicles are similar to typical internalized desmosomes described for epithelial and myocardial cells (45, 46).

DISCUSSION

Attachment of IF to desmosomal plaques is a special interaction of a cytoplasmic filament system with a specific plasma

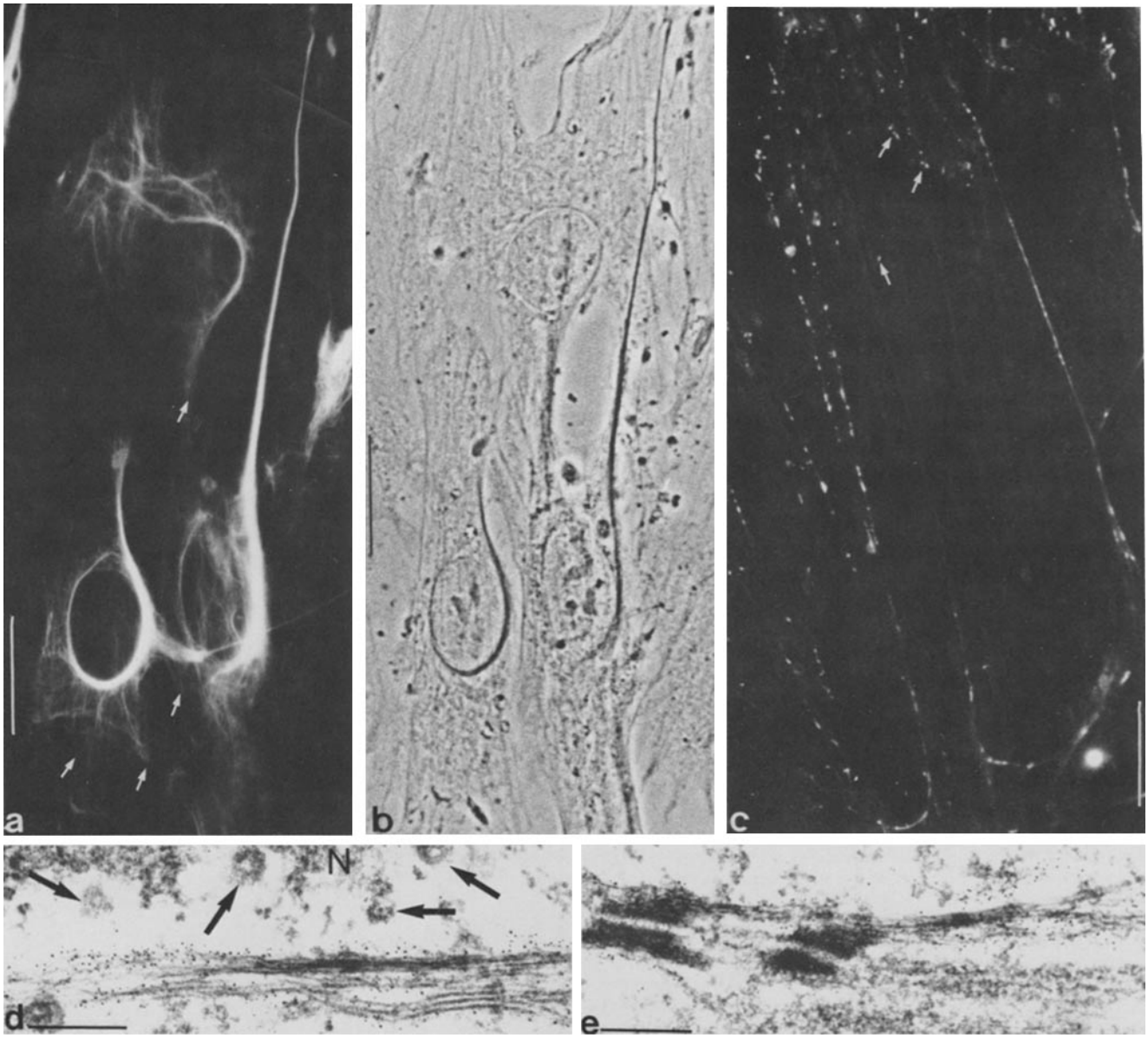

FIGURE 5 Meningioma cells in culture. Immunofluorescence microscopy (*a–c*) and immunoelectron microscopy (*d* and *e*) using antibodies to vimentin (*a*, *d*, and *e*) and to desmoplakins (*c*). Vimentin antibodies show extended arrays of IF in these cultured cells. In some cells most of the vimentin filaments are concentrated in a juxtanuclear whorl but also extend to elongated cellular projections. Only very small bundles of IF extend to the cell periphery (arrows in *a*). The massive bundles of IF can also be detected by phase-contrast microscopy (*b*). Immunofluorescence microscopy using antibodies to desmoplakin is shown in *c*. Most of the antigen is located at the cell periphery on desmosomal complexes. Fluorescent dots distributed over the cytoplasm most probably represent internalized desmosomal material (arrows, see also Fig. 6*c*). Immunoelectron microscopy using antibodies to vimentin, visualized by second antibodies coupled with 5 nm gold particles, shows a bundle of vimentin IF close to the nucleus (*N*, *d*), and IF bundles associated with desmosomal plaques (*e*). Arrows in *d* point to nuclear pore complexes. Bars, 20 μm (*a–c*); 0.3 μm (*d* and *e*). (*a* and *b*) × 910; (*c*) × 810; (*d*) × 50,000; (*e*) × 47,000.

membrane domain. Its specificity is also apparent from the exclusion of components associated with other kinds of junctions such as actin-containing microfilaments and vinculin which are specific for junctions of the *adhaerens* type (32, 33, 71). Desmosome-attachment is a characteristic feature of IF of the cytokeratin type and the protein components of these structures (e.g., desmoplakins and other desmosomal proteins and various combinations of cytokeratin polypeptides) are generally co-expressed. Absence of such desmosomal proteins has been noted in most nonepithelial cells and tumors, suggesting that expression of these proteins is correlated with epithelial differentiation. However, junctional structures resembling epithelial desmosomes have also been described in a great many nonepithelial cells, and it was difficult to assess the relationship of these junctions to epithelial desmosomes (for discussion see references 12, 14, and 36). Until recently the characterization of junction structures was exclusively based on morphological criteria. Recent identification of molecular components specific to certain junctions and the availability of antibodies to such proteins has allowed a biochemical definition of true desmosomal structures (4, 6, 25, 29). We have recently shown that the interaction of IF with

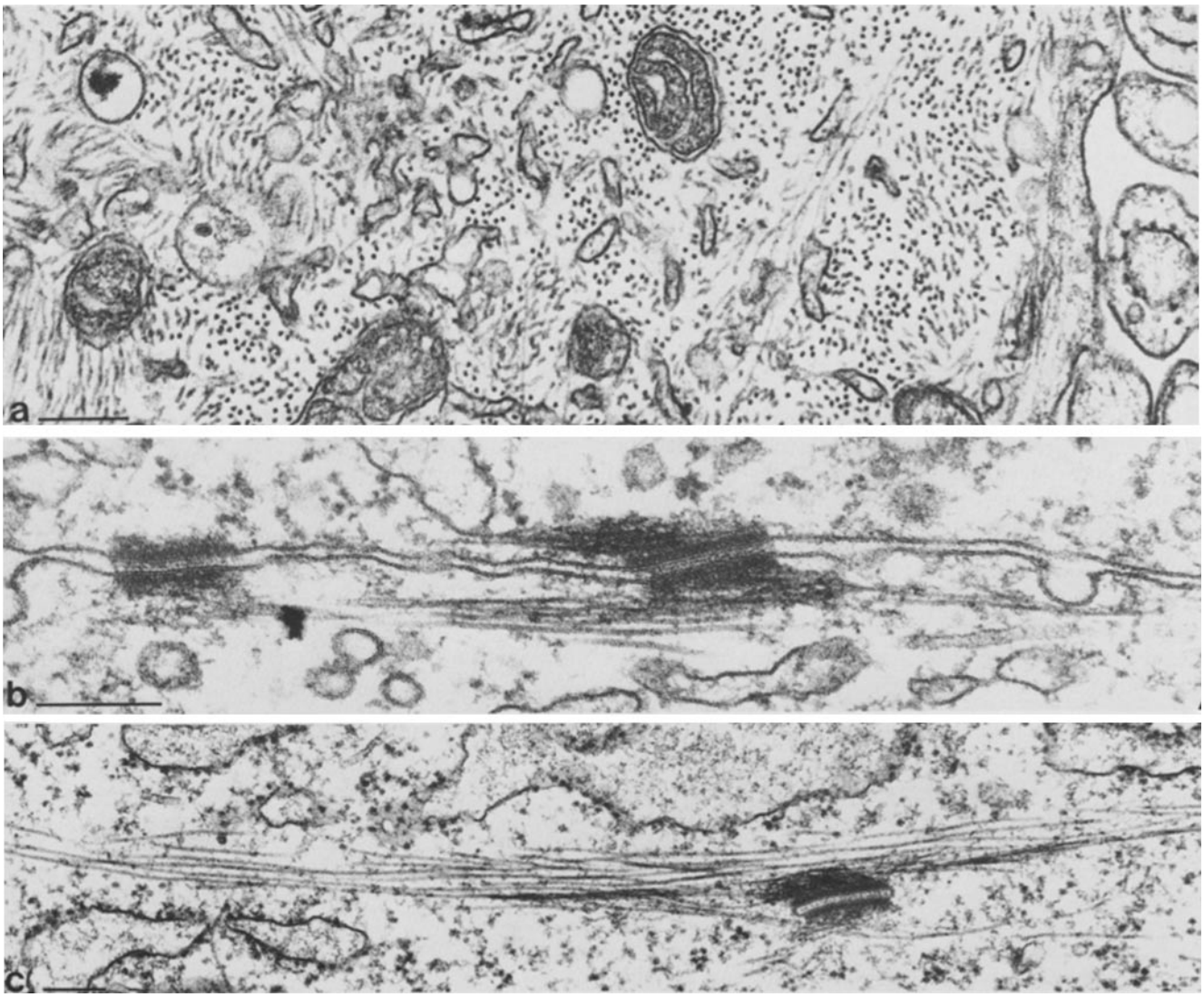

FIGURE 6 Electron micrographs of thin sections through meningioma cells in culture fixed as intact cells. A region showing cross sectioned IF (*a*) demonstrates the abundance of these filaments and the inter-IF distances, which is a characteristic feature of vimentin filament bundles (c.f. reference 27.). Often, the IF bundles laterally attached to the desmosomal plaques connect adjacent desmosomes (*b*). Cross-sectioned internalized desmosomal structures often represent a distinct midline, and desmosomal plaques with associated filaments (*c*). Bars, 0.2 μm. (*a*) × 68,000; (*b*) × 85,000; (*c*) × 50,000.

desmosomal plaque structures is not restricted to filaments of the cytokeratin type but that IF of the desmin type attach to the desmosomal plaques of myocardial cells and Purkinje fibers (46, 72; cf. 11). In this study we present the first example of the interaction of desmosomal plaques with a third type of IF, i.e., vimentin. Specific association of vimentin filaments with desmosomal plaques has been recognized in meningiomas, arachnoidal tissues, and in cell cultures derived from meningiomas. The fact that now three types of IF are known to specifically anchor at desmosomes but not on other plasma membrane domains, including junctions of the *adhaerens* type, indicates that the capability of anchorage at desmosomal plaques is a feature common to different types of IF. At present it is not known which of the desmosomal proteins are involved in IF anchorage.

This observation is in line with reports showing homologies in amino acid sequences of vimentin, desmin, and certain epidermal keratin polypeptides (34, 35, 42, 43, 69, 74), as well as common immunological determinants (58). Interestingly most of the homologous regions of the different IF proteins lie in their α-helical core positions (9, 35, 43, 68) which may suggest it is this core region that governs the association with the plaque proteins.

Co-existence of IF types such as vimentin and cytokeratin has been reported for various epithelial cells in culture that can form desmosomes (19–23, 26, 63, 73). Typically, in many of these cell lines the distribution of vimentin IF is different from that of the cytokeratin IF: whereas cytokeratins are constitutively attached to desmosomes, vimentin filaments frequently are confined to "free" margins of cells located away from intercellular contacts (e.g., 21, 26). This indicates that in such cells vimentin IF do not have the same chance for association with desmosomal plaques as cytokeratin IF, suggesting that different types of IF proteins may have different affinities to desmosomal plaque proteins.

The reported co-existence of desmosomal structures and proteins together with vimentin IF in cells lacking any cytokeratins reveals an unusual and rare combination of cyto-

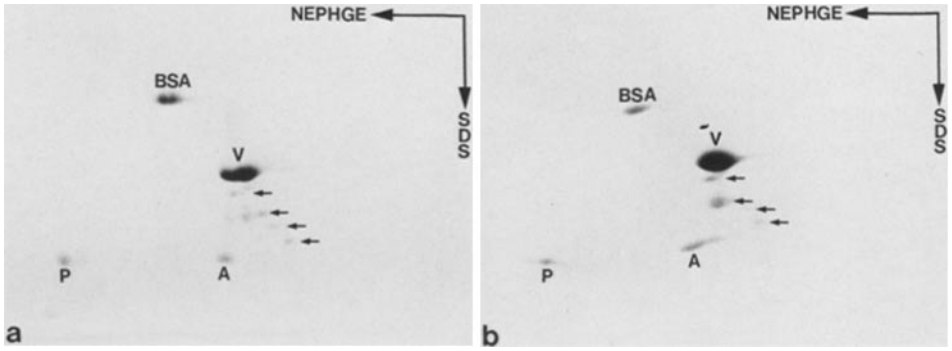

FIGURE 7 Two-dimensional gel electrophoresis of cytoskeletal preparations from meningiomal (*a*) and arachnoidal tissue (*b*) using nonequilibrium electrophoresis (*NEPHGE*) in the first dimension (*SDS*, direction of electrophoresis in the second dimension in the presence of SDS). Coomassie Blue staining reveals the predominant enrichment of vimentin polypeptides in both preparations. The arrows denote degradation products of vimentin. *A*, actin; *BSA*, bovine serum albumin; *P*, phosphoglycerokinase; *V*, vimentin.

skeletal components. Co-expression of desmosomal plaque proteins and vimentin seems to define a new class of cells (desmofibrocytes) that on the one hand, like fibroblasts, produce collagen type I and express vimentin IF but on the other hand, like epithelial and cardiac cells, express desmosomal plaque proteins at the same time. Our results show that such desmofibrocytes are present in normal human arachnoidal tissue and in meningiomas. We can, of course, not exclude the existence of this cell type in other hitherto undiscovered locations of the body. In a recent publication, Frank et al. (16) have reported the existence of cytokeratins in a certain cell culture believed to be derived from human arachnoidal cells in culture. Although we have not observed in arachnoidal or meningiomal tissue any cytokeratins in appreciable amounts we cannot exclude the existence of cytokeratin-positive cells as a minor cell population somewhere in the arachnoidal tissue.

Our results indicate that meningiomas of various types all originate from a special cell type, i.e., desmofibrocytes that form essential parts of the arachnoidal tissue. The presence of desmosomes distinguishes these cells from endothelial cells and fibroblasts present in peripheral regions of brain. The characteristic cytoskeletal features of this unusual cell type might provide a useful diagnostic criterion, and antibodies to desmoplakins and vimentin might help in deciding in the controversial discussion as to the nature and origin of some brain tumors, especially of the various forms of meningiomas (e.g., 3, 48, 70).

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