9 Nonvillous Parts and Trophoblast Invasion

H.G. Frank and P. Kaufmann

The nonvillous parts of the placenta include the chorionic plate, cell islands, cell columns, placental septa, basal plate, marginal zone, and fibrinoid deposits in all parts of the organ (Figure 9.1). As they are not vascularized by either the maternal or fetal circulations, they do not participate in maternofetal exchange. Irrespective of their heterogeneous location and structure, the nonvillous parts of the placenta have the same basic components (Figures 9.2A,B): extravillous trophoblast, fibrinoid, and, only in some locations, decidualized endometrial stroma. These components structurally and functionally do not vary from one nonvillous part to another. Therefore, these basic tissues are considered first.

Extravillous Trophoblast

HISTORICAL ASPECTS AND NOMENCLATURE

Placentologists have known for a long time that different cell types exist in the nonvillous parts of the placenta and that they differ markedly in shape and staining patterns. In particular, the large, intensely basophilic staining cells of all nonvillous areas have raised an enormous interest. Scipiades and Burg (1930) first employed the term “X cells,” the name implying that their origin was in dispute. The search for Barr bodies (sex chromatin, the heterochromatic second X chromosome of females) in X cells gave conflicting results (maternal origin: Klinger & Ludwig, 1957; fetal origin: Zhemkova, 1960). Systematic radioautographic studies on 3H-thymidine incorporation (Kim & Benirschke, 1971), as well as detailed structural (Kaufmann & Stark, 1971) and enzyme histochemical analyses (Stark and Kaufmann, 1971), gave clear evidence that X-cells are trophoblastic in nature. Final proof for the trophoblastic, fetal origin of the X-cells was obtained by Y-specific fluorescence in X-cells of placentas from male infants (Faller & Ferenci, 1973; Khudr et al., 1973). Systematic radioautographic studies on 3H-thymidine incorporation (Kim & Benirschke, 1971), as well as detailed structural (Kaufmann & Stark, 1971) and enzyme histochemical analyses (Stark and Kaufmann, 1971), gave clear evidence that X-cells are trophoblastic in nature. Final proof for the trophoblastic, fetal origin of the X-cells was obtained by Y-specific fluorescence in X-cells of placentas from male infants (Faller & Ferenci, 1973; Khudr et al., 1973; Maidman et al., 1973; Steininger, 1978).

Today, it is generally acknowledged that antibodies against cytokeratin, an epithelial intermediate filament, can be used as an easily applicable immunohistochemical marker of trophoblast (Khong et al., 1995). This antigen is not trophoblast specific but rather is expressed by all cells of epithelial origin. Because of this, in the nonvillous parts of the placenta, the amnionic epithelium and residual maternal glandular epithelium also are cytokeratin positive; moreover, some placental syncytiotrophoblast cells show a similar “intermediate” phenotype (Kurman et al., 1984a,b). Descriptions such as “intermediate trophoblast of the villous sprouts” (Pampfer et al., 1992) or “intermediate trophoblast cells at both villous and extravillous sites” (Riley et al., 1992) illustrate how confusing this term can be.

Extravillous Trophoblast Is a Tissue of Its Own

Most cellular and syncytiotrophoblast from the previl­lous stages of placentation are consumed for the devel-
Development of the placental villi. Here it forms the villous cytotrophoblast (Langhans' cells, the inner layer of the villous surface epithelium) and the villous syncytiotrophoblast (syncytium, the superficial layer, i.e., facing the intervillous space). The remaining trophoblast that is not consumed for villus formation deserves the name extravillous trophoblast and is the basic material for the development of all nonvillous parts to the placenta: chorion laeve, the marginal zone, chorionic plate, basal plate including cell columns, septa, and cell islands. Although extravillous trophoblast is present in such a variety of locations, its general structural and functional features are surprisingly homogeneous.

Extravillous trophoblast cells are epithelia in origin, but except for a few proliferative stem cells, they do not form a real polarized epithelial layer. Rather, after leaving the basal lamina facing the chorionic/villous stroma, the extravillous trophoblast cells achieve an interstitial phenotype (see Figure 9.1). This process has been analyzed ultrastructurally and immunohistochemically in much detail in the rhesus monkey (Enders, 1995, 1997a,b). Normal epithelia either secrete extracellular matrix in a polarized manner (basal lamina) or secrete no extracellular matrix at all (postproliferative cells of stratified epithelia). The same is valid for villous trophoblast. By contrast, the extravillous trophoblast cells secrete ample extracellular matrix as soon as they have left the cell cycle (Frank et al., 1994; Huppertz et al., 1996). Interestingly, this extracellular matrix is deposited in an apolar fashion as this usually is done by mesenchymal derivatives: no two-dimensionally organized basal lamina sheets are formed; rather, the matrix molecules accumulate extracellularly in large, three-dimensional patchy aggregates completely embedding the extravillous trophoblast (matrix-type fibrinoid; see following).

Typically, this apolar matrix is secreted in the direct vicinity of maternal tissues, that is, facing the maternal blood (e.g., cell islands, intervillous surface of the chorionic plate, placental septa) or maternal decidua (basal plate with cell columns, chorion laeve). As a consequence...