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The localization of Thy-1.1, MRC OX 2 and Ia antigens in the rat ovary and fallopian tube

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Summary. The localization of Thy-1, MRC OX 2 and Ia antigens as defined by monoclonal antibodies MRC OX 7, MRC OX 2 and MRC OX 6 was determined by an indirect immunoperoxidase technique on cryostat sections of rat ovaries. Thy-1 antigen was present significantly in the theca interna of growing antral follicles. Developing corpora lutea exhibited an increasing presence of Thy-1 antigen and it was still present in degenerating ones. Thy-1 antigen was constantly present in fallopian tube tunica propria. The MRC OX 2 antigen was expressed most on ovarian structures that do not develop further, i.e. granulosa of degenerating antral follicles and third generation of corpora lutea. MRC OX 2 antibody stained the capillaries of the fallopian tube; the most heavily MRC OX 2^+ were the cells of ovarian germinal epithelium. The Ia^+ cells were occasionally found within the growing ovarian structures but they were more frequent in degenerating ones. Rare or no Ia^+ cells within the ovary and heavily Ia-depleted thymus medulla and Ia areas in the spleen were, however, observed in some rats. The role of these antigens with respect to the structures they label is discussed.

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INTRODUCTION

The contemporary neuro-endocrine concept of ovarian function control fails to explain a number of events of ovarian physiology (Richards, 1979). A possibility has been offered that the immune system interferes in this process (Bukovský & Presl, 1979; Bukovský, Presl & Holub, 1981a). We have recently localized the Thy-1 antigen within the rat ovary (Bukovský, Presl, Holub, Mančal & Krabec, 1982c).

The Thy-1 (theta) antigen described in mice by Reif & Allen (1964) as an antigen common to brain and thymus was also found in rats as Thy-1.1 alloantigen in all strains (Douglas, 1972). In rats most T lymphocytes lack Thy-1 (Acton, Morris & Williams, 1974) and the molecule was found on a subset of bone marrow cells (Williams, 1976). In rodents some fibroblasts, epidermal cells, breast cells and muscle cells also display Thy-1 antigen (reviewed in Campbell, Gagnon, Reid & Williams, 1981). Some lymphocytes, reticular cells and pericytes of blood vessels in rat spleen and lymph node exhibited Thy-1 (Barclay, 1981) and recently the Thy-1 antigen was also described in rat kidney glomeruli (Bukovský, Presl, Holub, Mančal & Krabec, 1981b; Barclay, 1981), within the pituitary and adrenal gland, and in a number of rat foetal tissues (Bukovský, Presl, Holub, Mančal & Krabec, 1982b; Bukovský, Presl & Židovský, 1982d). The carbohydrate composition obtained for brain Thy-1 glycoprotein molecules

strikingly differs from that found for the molecule from thymocytes (Barclay, Letarte-Muirhead, Williams & Faulkes, 1976) and an apparent sequence and structural homology of Thy-1 glycoprotein with immunoglobulin was described (Campbell, Williams, Bayley & Reid, 1979; Cohen, Novotný, Sternberg, Campbell & Williams, 1981). Thy-1 antigen has been suggested as a member of a set of molecules related to the Ig domain that mediate cell interactions in a manner analogous to the set of domains mediating Fc functions of Ig; the involvement of Ig-related structures in tissue interactions was, however, qualified as more primitive than their involvement in the immune system (Cohen *et al.*, 1981). To approximate the possible role of Thy-1 antigen within the ovary a detailed study using the monoclonal antibodies was undertaken. Simultaneously the MRC OX 2 and Ia antigens were studied. The MRC OX 2 antigen (thymocyte glycoprotein) is also present in thymus and nervous tissue (McMaster & Williams, 1979a) but in the spleen it occupies areas different from Thy-1 antigen (Barclay, 1981). The Ia antigen is a product of the major histocompatibility complex (McMaster & Williams, 1979a) and it was detected on bone marrow-derived dendritic cells in the T-dependent areas of rat spleen and lymph nodes in addition to B cells (Barclay, 1981).

MATERIALS AND METHODS

Rats

Three-month-old outbred virgin female Wistar rats of our laboratory colony with a regular 4-day cycle were reared in cages illuminated for 14 hr (05.00–19.00 hr). One or two animals were studied at 6 hr intervals during the ovarian cycle starting from oestrus 03.00 hr (day 1) and finishing on proestrus, 21.00 hr (day 4).

Antibodies

The following mouse anti-rat monoclonal antibodies were used: MRC OX 7 (anti-Thy-1.1; Mason & Williams, 1980), MRC OX 2 (anti-thymocyte glycoprotein; McMaster & Williams, 1979a) and MRC OX 6 (anti-Ia; McMaster & Williams, 1979b). Monoclonal antibodies were used as ascitic fluid of mice bearing hybridoma cells and were the generous gift from Dr A. F. Williams (University of Oxford, Oxford).

Peroxidase-conjugated antibodies

Swine IgG anti-mouse 7 S Ig (Sevac, Prague) was coupled to horseradish peroxidase essentially by the method of Wilson & Nakane (1978). Horseradish peroxidase (Boehringer, Mannheim, catalogue number 108090 grad I, RZ ~ 3) 4 mg in 1 ml of H_2O was reacted with 0·2 ml of freshly made 0·1 M $NaIO_4$. The mixture was stirred 20 min at 20° and then passed through a K 9/15 column (Pharmacia, Sweden) of Sephadex G-25 medium. Activated peroxidase was reacted with 8 mg of swine IgG anti-mouse 7 S Ig in 1 ml of 0·01 M carbonate buffer, pH 9·5 and 0·05 ml of 0·2 M carbonate buffer, pH 9·5 for 2 hr with stirring at 20°. 0·1 ml of fresh sodium borohydride (4 mg/ml of H_2O) was added and incubated 2 hr at 4°. An equal amount of saturated ammonium sulphate solution was added and the precipitate (after centrifugation) was washed twice with 50% saturated ammonium sulphate and centrifuged again. The precipitate was dissolved in a minimal amount of H_2O and passed through a K 9/15 column of Sephadex G-25 in PBS, pH 7·2. Protein concentration was about 8 mg/ml, 1 mg of NaN_3/ml was added as preservative; this amount of NaN_3 did not inhibit the activity of the high concentration of peroxidase coupled to antibody. The conjugate stood until use at 4°.

Localization on tissue sections

Fresh ovaries (and spleens and thymuses of the same rats) were frozen on dry ice and stored at −20° until sectioned. Six micrometre cryostat sections were air dried for 1 hr at 20° and overnight at 4° before fixation in acetone at 20° for 5 min. Fixed, air-dried sections were then washed shortly with PBS, pH 7·2 and covered with the specific antibodies diluted 1 : 100 with PBS. Controls consisted either of normal mouse IgG diluted 1 : 100 or PBS in the first step and the same procedure mentioned below. After 30 min in a moist chamber at 20° the monoclonal antibodies were washed from slides (3 × 10 min) with PBS and the slides were covered with azid-H_2O_2 solution (1 mg of NaN_3/15 ml of PBS with 0·17 ml of 0·5% H_2O_2) for 10 min. The sections were then washed (3 × 10 min) in PBS and incubated with peroxidase-conjugated antibody for 20 min at 20°. Before incubation with sections the peroxidase-labelled antibody was diluted 1 : 20 with PBS, incubated with rat testis homogenate (300 mg of homogenate was added to each ml of diluted antibody) for 10 min to remove non-specific staining, and centrifuged for 20 min at 20° (16,000 ***g***). The unbound peroxidase-conjugated antibody was washed (2 × 10 min with PBS and 1 × 10 min with 0·02 M Tris-HCl, pH 7·6) from slides and the peroxidase on sections was revealed by reacting with 3·3′ diamino-

Table 1. Localization of Thy-1, MRC OX 2 and Ia antigens in the rat ovary

Ovarian tissue	Thy-1	MRC OX 2	Ia
Vital antral follicles			
Theca interna	'Spike-like' structures increase with the follicular growth up to the complete 'ring' attached to the follicular basal membrane; focal expression of heavily stained cells	Lightly stained 'ring' of cells attached to the follicular basal membrane in large antral follicles	Infrequent Ia cells
Granulosa	Traces ('spikes') in basal layers of large follicles diffused from adjacent thecal 'ring'	Absence or light diffuse staining in large follicles	Not detected
Degenerating (atretizing) antral follicles			
Theca interna	Infrequent cells and focal distribution of 'spikes'	Focal stained cells	Frequent Ia cells
Granulosa	Positive structures not detected	Often heavy staining of all cells	Ia cells sometimes present
Corpora lutea of the first generation, i.e. those developing in the actual cycle			
	'Spike-like' structures in basal layers of granulosa-luteal cells; occasional heavily stained cells	Light diffuse staining more expressed in the sites corresponding to Thy-1 antigen	Frequent Ia cells amongst theca-luteal cells; occasional amongst granulosa-luteal cells
Corpora lutea of the second generation, i.e. those developed in the previous cycle			
	Frequent positive cells; intercellular 'spikes' diffuse throughout the parenchyma	Light staining of endothelia of capillaries	Focal distribution of Ia cells throughout the parenchyma
Corpora lutea of the third generation, i.e. those developed two cycles ago			
	Frequent positive cells with tendency to lysis, sometimes 'spike-like' structures intercellularly	Frequent heavily positive cells probably also corresponding to Thy-1 positive cells	Frequent Ia cells
Ovarial germinal epithelium			
	Rare 'spikes' and rare heavily stained cells beneath the epithelium	Almost constant heavy staining of epithelium	Relation of Ia cells is not evident
Fallopian tube			
Epithelium	Not detected	Not detected	Sometimes traces
Tunica propria	Heavy diffuse staining of intercellular 'spikes', some positive cells	Capillaries	Sometimes occasional Ia cells
Ovarian stroma (interstitium) and mesosalpinx, fallopian tube smooth muscle			
	Pericytes of vessels and sometimes the presence of Thy-1 positive material among the endothelia; different amounts of positive cells; nerves	Capillaries, endothelia of vessels; different amounts of positive cells; sometimes diffuse staining of various density of ovarian intersticium	Variable amounts of Ia cells but in some rats rare or absent

benzidine tetrahydrochloride (Fluka, A.G., catalogue number 32750) for 4–6 min as described by Graham & Karnovsky (1966). The slides were slightly counterstained with Harris's haematoxilin and evaluated in an Amlival photomicroscope (Carl Zeiss, Jena) using the SIF 486 (blue) or SIF 551 (green) selection interference filters.

RESULTS

Ovary and fallopian tube

The results of localization of Thy-1, MRC OX 2 and Ia antigens are summarized in Table 1. Further details are given in the figure legends and below. Controls using normal mouse IgG or PBS in the first step gave insignificant levels of non-specific staining of some fibrous tissue (mainly in ovarian stroma). The occasional cells (mainly polymorphonuclear leucocytes), the ovarian follicular fluid and the coagulated plasma of vessels were also non-specifically stained (Figs 1D, 3D and 3G).

Localization of Thy-1 antigen

Rare Thy-1$^+$ cells were found in connection with preantral follicles. Antrum formation and follicular growth were associated with the presence of Thy-1$^+$ cells and structures in theca interna (Fig. 1A) and particularly in the neighbourhood of the follicular basal membrane (Fig. 2A). The characteristic Thy-1$^+$ 'spikes' (Bukovský, Presl, Holub, Mančal & Krabec,

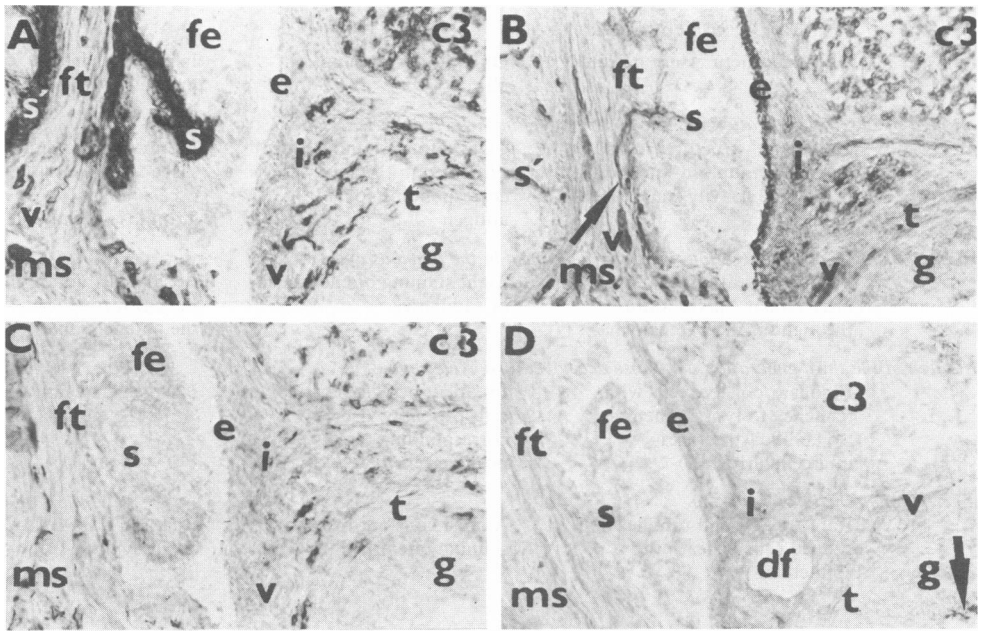

Figure 1. Ovary (right) and fallopian tube (left) (metoestrus 09.00 hr). (A) The anti-Thy-1 antibody stains some cells and structures within the theca (t) of medium growing antral follicle and many in degenerating corpus luteum of the third generation (c3), pericytes of vessels (v) and the nerves in ovarian intersticium (i) and mesosalpinx (ms) of the fallopian tube (ft). There is a heavily stained submucosa (tunica propria) of the fimbriae (s) and endosalpinx (s'). Note the unstained fallopian tube epithelium (fe), the ovarian germinal epithelium (e) and granulosa (g) of the follicle. (B) The MRC OX 2 antibody stains some cells in theca and many in degenerating corpus luteum, endothelia of the vessels including capillaries of fallopian tube tunica propria and smooth muscle (arrow). No staining of the fallopian tube epithelium but heavy staining of ovarian germinal epithelium and lightly diffusely stained ovarian interstitium and granulosa of the follicle are evident. (C) The anti-Ia antibody stains sporadic cells in the theca of growing follicle but more frequent cells in the degenerating corpus luteum and in ovarian interstitium. There are some positive cells in mesosalpinx and smooth muscle but there is no staining of tunica propria and only traces in the fallopian tube epithelium. There is no staining of ovarian germinal epithelium and granulosa of the follicle. (D) Control gives non-specific staining of follicular antral fluid (arrow) and low level of label among cells of corpus luteum and ovarian and fallopian tube interstitium. A degenerating (atretizing) small follicle (df) is also present in this section. The cells are unlabelled and only the counterstaining of the nuclei is visible. (Magnification × 150).

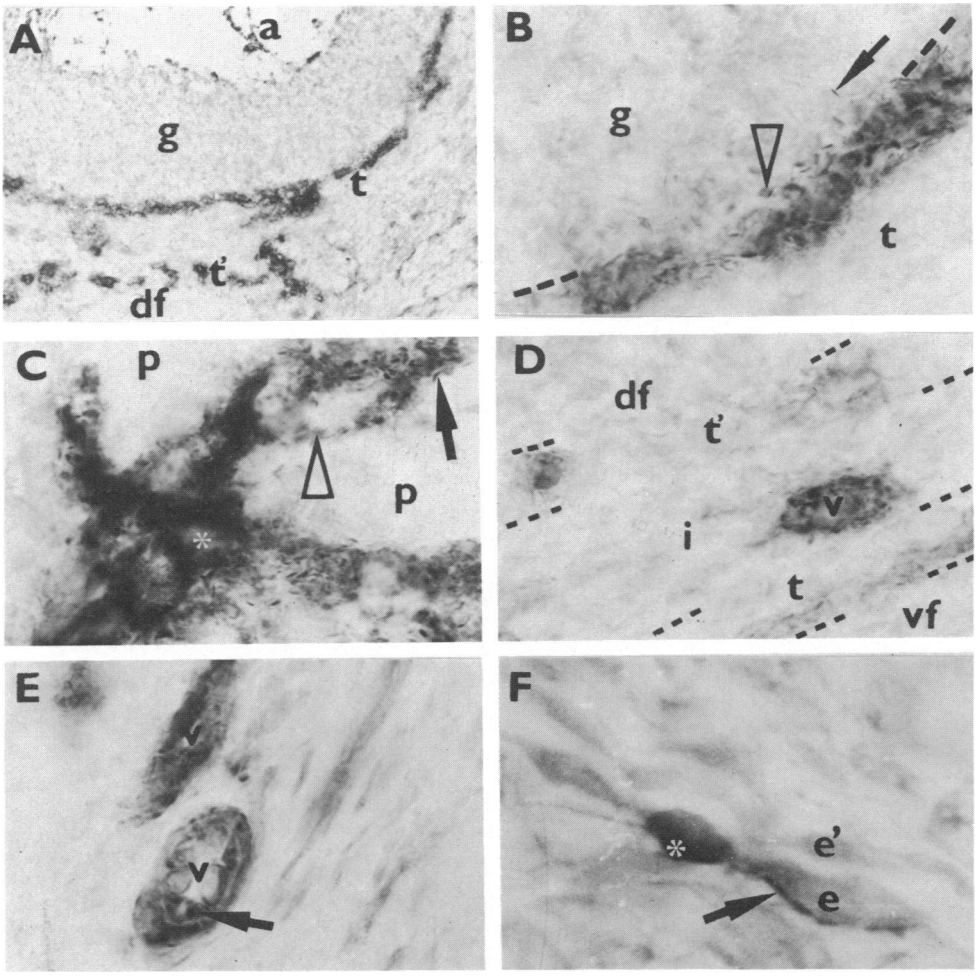

Figure 2. (A) Ovary (prooestrus 15.00 hr). The anti-Thy-1 antibody stains the complete 'ring' of the theca(t) cell layer attached to the follicular basal membrane while the granulosa (g) of a growing preovulatory antral follicle exhibited no evident staining. There is, however, the non-specific label of antral fluid (a) (compare with Fig. 1D). A small degenerating (atretizing) antral follicle (df) with diminished granulosa-cell layer exhibited focal Thy-1$^+$ cells in persistent theca (t'). (B) At higher power, the intercellular 'spike-like' Thy-1$^+$ structures (arrow) and the lightly stained 'vesicles' (empty arrow) in the basal layer of granulosa cells are demonstrated. Note that the Thy-1$^+$ structures (arrows) derived from the thecal 'ring' are released in one way through the follicular basal membrane (indicated by dashed lines) among the granulosa cells but not among the deeper thecal cells. (C) The corpus luteum of the second generation (early stage metoestrus 03.00 hr). The anti-Thy-1 antibody stains the 'spike-like' structures (arrow) and vesicles (empty arrow) diffusing intercellularly throughout the parenchyma (p), the heavily stained cells (asterisk) are also present. (D) Ovary (oestrus 03.00 hr). A vital medium antral follicle (vf) expressing the Thy-1$^+$ continuous 'ring' in the theca (t) cell layer attached to the follicular basal membrane and a degenerating (atretizing) large antral follicle (df) exhibiting only focal Thy-1$^+$ cells and structures in the theca (t'). Thecal borders of both follicles are indicated by dashed lines. Note the small vessel (v) in the interstitium (i) with the Thy-1$^+$ material. (E) Ovarian interstitium (metoestrus 09.00 hr). Thy-1$^+$ vessels (v). Note the Thy-1$^+$ material (arrow) among the Thy-1 negative endothelia. (F) Two sheets of invaginated ovarian germinal epithelium (oestrus 03.00 hr). The Thy-1$^+$ cell (asterisk) is attached to the epithelial cell and the 'spike-like' Thy-1$^+$ material (arrow) is present on one sheet (e). Note the smaller cells of the other sheet (e'). Magnification A × 150; B, C, D, E × 920; F × 2,240. MRC OX 7 antibody.

1982a), but not Thy-1$^+$ cells, were found sometimes to invade basal parts of the granulosa-cell layer through follicular basal membrane from the adjacent theca interna of growing antral follicles (Fig. 2B). In contrast, degenerating (atretizing) antral follicles exhibited low amounts of Thy-1$^+$ material in follicular theca and none in granulosa (Fig. 2D). Within the corpora lutea of the first generation, i.e. those developed in the actual cycle, the Thy-1 antigen was observed within the basal layers of the granulosa-luteal cells up to the end of the cycle (Fig. 3A). In the following cycle the corpora lutea of the second generation exhibited at first the net-like Thy-1 positivity, probably partly corresponding to pericytes of developing vessels, in advanced stages the Thy-1$^+$ 'spikes' diffused throughout the tissue (Figs 2C and 3E). With the beginning of degeneration the third generation of copora lutea collapsed mainly due to the loss of parenchymatous cells and the contracted stroma usually exhibited a degeneration of Thy-1$^+$ cells. Pericytes of some vessels in ovarian interstitium, but sometimes also some structures among endothelia (Figs 2D and 2E), were also Thy-1$^+$. Below the ovarian germinal epithelium the Thy-1$^+$ cells and 'spikes' were occasionally found (Fig. 2F). The fallopian tube tunica propria was constantly Thy-1$^+$ (Fig. 1A).

Localization of MRC OX 2 antigen

Preantral follicles were unstained while a small amount of MRC OX 2 antigen was usually present on some thecal cells of antral follicles (Fig. 1B), probably corresponding to Thy-1$^+$ cells. Granulosa of vital antral follicles was weakly stained (Fig. 1B) or unstained (Fig. 4F) whilst the granulosa of degenerating large antral follicles was sometimes heavily MRC OX 2$^+$ (Fig. 4F). Corpora lutea of the first generation

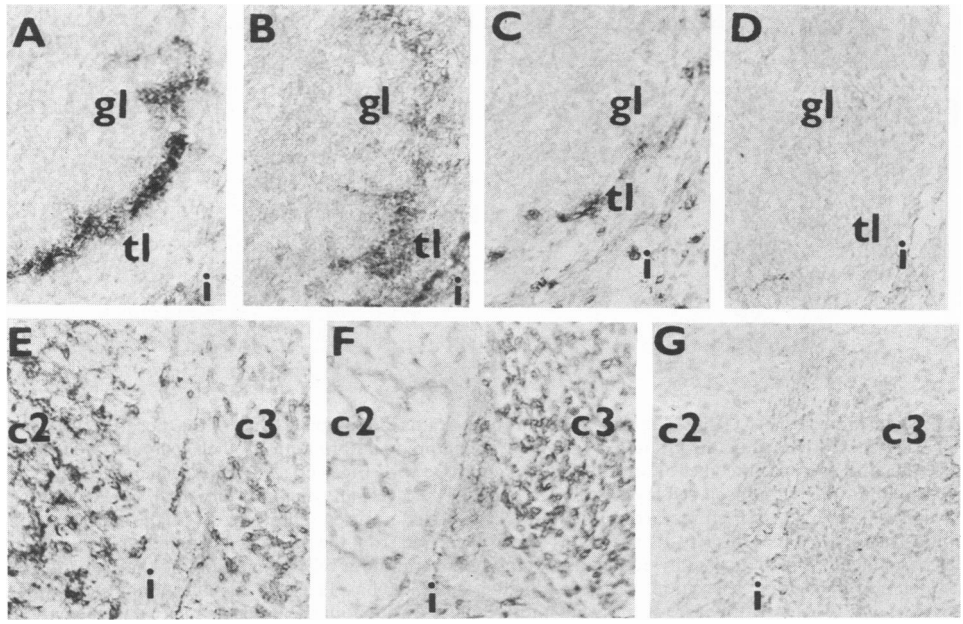

Figure 3. Corpus luteum of the first generation (late stage prooestrus 09.00 hr): (A) The anti-Thy-1 antibody stains the basal layers of granulosa-luteal cells (gl), there is no staining of theca-luteal cells (tl) but of some positive cells in the interstitium (i); (B) The MRC OX 2 antibody gives a light diffuse staining which is more expressed in the sites corresponding to the presence of Thy-1 antigen on the granulosa-luteal cells, some MRC OX 2 positive cells in the interstitium are also present; (C) The anti-Ia antibody stains cells which are more frequent among the theca-luteal cells and in the interstitium, some positive cells are present in the basal granulosa-luteal layers; (D) control shows counterstain with only a low level of non-specific staining. Corpora lutea of the second (c2) and third (c3) generation (late stages dioestrus 21.00 hr); (E) the anti-Thy-1 antibody stains almost diffusely the parenchyma of c2, many stained cells in c3 and rare positive cells in interstitium are present; (F) the MRC OX 2 antibody stains lightly capillaries in c2 while there are heavily stained numerous cells in c3, infrequent cells are present in interstitium; (G) control shows a low level of non-specific staining. (Magnification × 150).

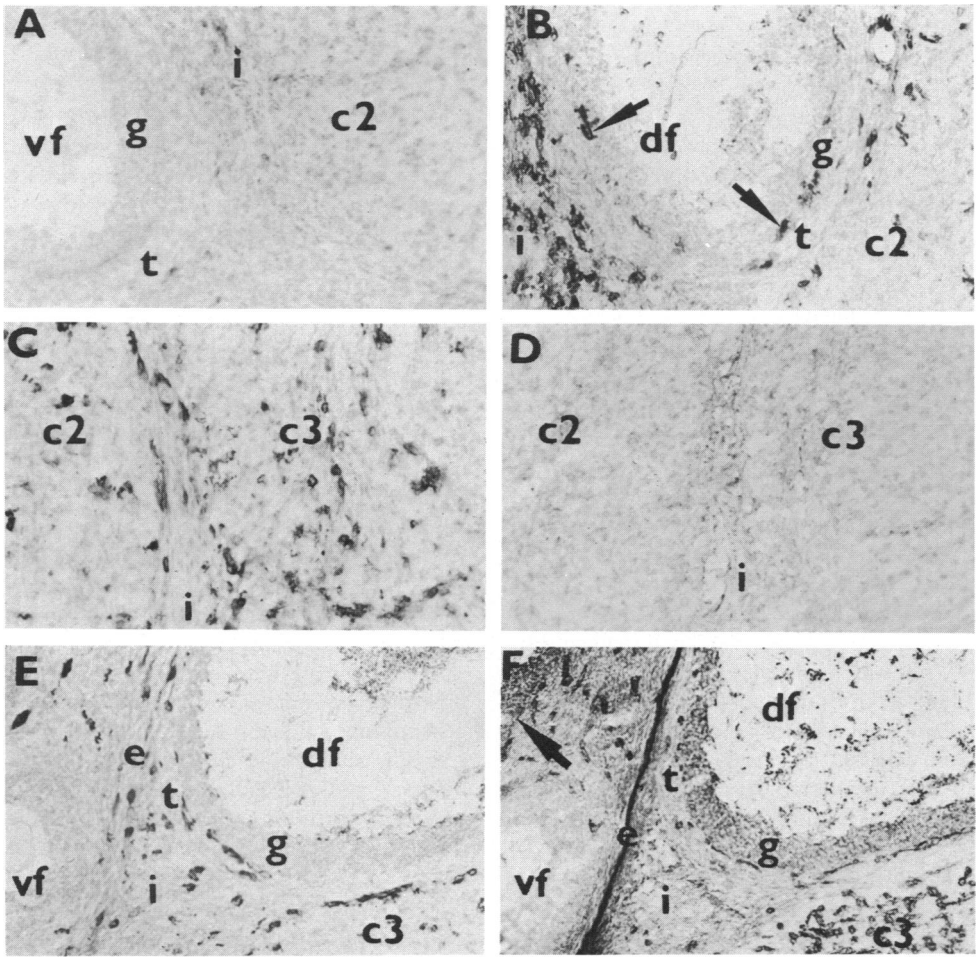

Figure 4. (A) Theca (t) and granulosa (g) of a vital (growing) antral follicle (vf) and corpus luteum of the second generation (c2) incubated with anti-Ia antibody (prooestrus 09.00 hr). Note the only traces of staining of some cells in the corpus luteum and ovarian interstitium (i). (B) Large degenerating (atretizing) antral follicle (df) and corpus luteum of the second generation of the prooestrous rat (15.00 hr), stained with anti-Ia antibody. The mass of Ia positive cells in the interstitium and frequent Ia cells in the theca of a degenerating (atretizing) follicle; the Ia cells even invade among the altered granulosa cells (arrows). Infrequent Ia positive cells in the corpus luteum. (C) Corpora lutea of the second and third (c3) generation (prooestrus 15.00 hr) stained with anti-Ia antibody. Occasional Ia positive cells in c2 and more frequent in c3 and interstitium. The same ovary as in (B). (D) Corpora lutea of the second and third generation in prooestrus (21.00 hr). The anti-Ia antibody produces only traces of staining in ovarian interstitium and almost no staining in both types of corpora lutea. (E) Small vital and large degenerating (atretizing) antral follicle (oestrus 03.00 hr). The anti-Ia antibody stains occasional cells in the interstitium and theca, but not in granulosa—compare with (B), of the degenerating follicle. The corpus luteum of the third generation exhibited frequent Ia-positive cells in the border with the interstitium and only infrequent ones in the parenchyma. No staining of a vital follicle and the germinal epithelium (e). (F) Parallel section to (E) stained with MRC OX 2 antibody shows infrequent positive cells in the interstitium and theca of a degenerating follicle. Note the heavy stained granulosa of degenerating follicles (the similar one is indicated by an arrow) but no staining of granulosa in the vital follicle. There are two heavily stained sheets of invaginated ovarian germinal epithelium and frequent positive cells in degenerating corpus luteum. (Magnification × 150).

exhibited low amounts of MRC OX 2 antigen on the sites corresponding to the presence of Thy-1 antigen (compare Figs 3A and 3B), in those of the second generation the endothelia were MRC OX 2^+, and in the corpora lutea of the third generation the cells, probably corresponding to Thy-1^+ cells, were stained with MRC OX 2 antibody (Fig. 3F and compare with 3E). Ovarian germinal epithelium was constantly heavily MRC OX 2^+ (Figs 1B and 4F). Within the fallopian tube tunica propria the vessel endothelia were MRC OX 2^+.

Localization of Ia antigen

Infrequent Ia^+ cells were found in theca interna of developing antral follicles (Fig. 1C); the amount of these cells was substantially increased in some degenerating antral follicles (Fig. 4E) and the Ia^+ cells in some rats even invaded the granulosa cell layer (Fig. 4B). The corpora lutea of the first generation exhibited frequent Ia^+ cells among the theca-luteal cells but only sporadic ones among the granulosa-luteal cells (Fig. 3C). In the corpora lutea of the second generation the Ia^+ cells were focally distributed but the corpora lutea of the third generation usually exhibited frequent Ia^+ cells sometimes with a tendency to cluster formations (Figs 1C and 4C). The occasional Ia^+ cells were found in fallopian tube connective tissue and the traces of Ia antigen were detected in its epithelium (Fig. 1C). It is interesting that there were ovaries exhibiting a very small number or no Ia^+ cells in some stages of rat ovarian cycle and periods of day (Figs 4A and 4D). Another rat investigated in the same period was, however, more positive (see Fig. 3C as compared with 4A).

Spleen and thymus

To compare the immune system changes during the ovarian cycle the spleens and thymuses of most rats were also investigated. There were no deep changes of the usual distribution of Thy-1 and MRC OX 2 antigens in the spleens and the picture was similar to that described (Barclay, 1981). Furthermore all rats exhibited almost a diffuse staining pattern with anti-Thy-1 and MRC OX 2 antibody in the thymuses. In contrast those rats exhibiting low or no Ia^+ cells in the ovaries have only traces of Ia antigen in spleen follicles, marginal zones and periarteriolar lymphocyte sheaths, in their thymuses the medulla was low in Ia antigen and only the thymic cortical reticular (interdigitating) cells exhibited almost the usual staining pattern with MRC OX 6 antibody.

DISCUSSION

This study expands the contemporary knowledge of distribution of Thy-1, MRC OX 2 and Ia antigens in the rat tissues. The role of these antigens is, however, unknown. We have recently suggested that Thy-1^+ intercellular structures ('spikes') may represent some promotive substance released *in situ* by Thy-1^+ transit cells which recognize tissue-specific antigens and thus control the target cell function (Bukovský *et al.*, 1982b). In the case of the ovary the constant amount of follicle-antigen-specific subpopulation of Thy-1^+ transit cells supplying the cohort of growing antral follicles may represent the essence of selective mechanism due to the reduction of the number of supported surface-enlarging follicles. Other follicles left are subjected to the effect of regressive factors, the character of which may vary during the ovarian cycle (Bukovský, Presl, Holub, Mančal & Krabec, 1982c). The developing corpora lutea were also found to exhibit an increasing amount of Thy-1^+ cells and 'spikes'. Corpora lutea have, in principle, their own built-in programme of life; as in the rat there are three generations in different developmental and functional stages together in each ovary. Their life can be, however, prolonged during pregnancy and pseudopregnancy, or after anti-thymocyte serum treatment (Bukovský, Presl, Krabec & Bednařík, 1977). In contrast to ovarian follicles and corpora lutea the fallopian tube tunica propria exhibited an almost constant amount of Thy-1^+ cells and 'spikes' associated with no distinct morphological changes of the epithelium. During rat ontogeny the fallopian tube exhibits Thy-1^+ cells and 'spikes' as one of the early (foetal) Thy-1^+ tissues, ovarian follicles later on (postnatally), and the corpora lutea as one of the latest (postpubertal) Thy-1^+ tissues (Bukovský *et al.*, 1982d; unpublished results). We propose that different pathways of tissue control exist depending on the time of tissue antigen appearance during the 'critical periods' of development (Presl, Bukovský & Krabec, 1979), as are the prenatal, postnatal and peripubertal periods in the rat. The Thy-1^+ 'spikes' released by Thy-1^+ transit cells migrating into the tissues from their sources in the organism (Bukovský *et al.*, 1982d) should be, however, distinguished from the proper diffuse Thy-1 expression corresponding to the attainment of tissue

maturity, e.g. diffuse Thy-1 expression in the mature brain and glomeruli (Bukovský *et al.*, 1982a) or on some breast cells in tissue culture (Dulbecco, Bologna & Unger, 1979).

The MRC OX 2 antigen perhaps stabilizes some target structures developed under the influence of Thy-1$^+$ transit cells and might prevent the tissue from further proliferation. Such an effect could be undesirable for follicular development and the follicle exhibiting distinctly MRC OX 2$^+$ granulosa cells can undergo degeneration. Moreover the heavily MRC OX 2$^+$ one-cell layered ovarian germinal epithelium should be unable to proliferate. On the other hand the distinctly MRC OX 2$^+$ cells in third generation corpora lutea are probably identical with Thy-1$^+$ transit cells. Thus the MRC OX 2 antigen could probably influence the functional capacity of Thy-1$^+$ transit cells and so, indirectly, influence the parenchymal cells of some tissues. Except for the vascular endothelia there were, however, no MRC OX 2$^+$ structures in the fallopian tube epithelium and tunica propria. The variability in Ia$^+$ cells suggests that this cell type may not be essential for developmental events in rat ovaries, and is more likely to be related to immune functions comparable with other Ia$^+$ dendritic cells (Thorbecke, Silberberg-Sinakin & Flotte, 1980). A transient weakening or loss of lymphocyte HLA antigens in healthy women during some periods of the ovulatory cycle was, however, also described (Májský & Jakoubková, 1976; Májský, Presl, Bukovský & Abrahámová, 1980). The distinct presence of Ia$^+$ cells in some degenerating ovarian structures might suggest the association with regressive effect of these cells.

In conclusion, we propose that the Thy-1, MRC OX 2 and Ia antigens are the components of a more complex tissue control system mutually connected with the immune system in adult individuals. Our idea coincides with the hypothesis on the role of Thy-1 antigen as one of a set of molecules that mediate cell interactions leading to tissue formation (Cohen *et al.*, 1981).

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