Supplemental Figure 3. Definitions assigned to distinguish pathologic lesions relevant to this project.

**Antral follicle degeneration**: antral follicles are less numerous and are categorized as such by their large size, large number of granulosa cells and a space in the middle usually filled with follicular fluid. They were classified as ‘degenerate’ when the antrum appeared larger than normal with the appearance of starting to form into a more cystic-like structure. Sometime hemorrhage is found in the antrum in older animals.

**Corpora lutea hypertrophy**: normal looking cells with an increase in number compared to normal CL. Can be difficult to distinguish from a small luteoma.

**Cystadenoma**: usually a unilateral cystic structure lined by cuboidal or columnar epithelium with papillary growths, lack of cilia on cell surfaces, large cytoplasmic vacuoles and are considered a common neoplasm in mice.

**Epithelial inclusion cyst**: Lined by single or multiple layers of columnar epithelium that form papillary structures projecting into the lumen. Usually age related lesions but are considered a precursor to adenoma.

**Follicular cyst**: These are also part of the degenerative process and usually have one to four layers of cuboidal granulosa cells. Their lumen may or may not contain blood, inflammatory cells, pale proteinaceous material, degenerating oocytes and large, sometime foamy macrophages.

**Follicular degeneration**: refers to the later stage of follicles influenced by it’s decreased responsiveness to pituitary hormones. They can be smaller in size with very few granulosa cells and are usually surrounded by interstitial tissue.

**Granulosa cell tumour**: Most frequently they are characterized by varying-sized follicles that compress adjacent tissue or completely efface the ovary. Follicles are composed of round to cuboidal cells arranged on a delicate basement membrane. Cell borders are usually discrete and the cytoplasm varies from scant to abundant. Cell nuclei are centrally-located and round, oval, indented, and have coarsely stippled chromatin. Mitotic figures vary from few to many. The cells often resemble granulosa cells of normal follicles. Occasionally, the pattern is more tubular. Malignant granulosa cell tumours invade the surrounding fat and bursae and may metastasize to the lungs, lymph nodes, and other tissues. These tumours are composed of pleomorphic, round to cuboidal cells, often arranged in sheets, occasionally forming discrete follicles. Mitotic activity is often high.

**Interstitial cell hyperplasia**: Usually found in aging ovaries. Typically concomitant with hypertrophy. Cells are enlarged with a pale eosinophilic foamy cytoplasm and had brown to yellow tinged pigment. Other cases can have large amounts of granular yellow-brown pigment. The most common pigment in these cells is ceroid and can be found in increased incidences with age.
**Luteoma**: can be based on size only as the neoplastic cells often appear similar to those in normal corpora lutea. It is frequently difficult to distinguish between luteal cell hyperplasia and smaller luteomas. Generally, they have sheets of follicles of round to polygonal cells with abundant pale eosinophilic vacuolated cytoplasm. The cells have oval nuclei and there are rare mitotic figures.

**Luteoma (small)**: as above, but with slight to severe compressions of surrounding tissue.

**Ovarian atrophy**: usually an ‘end-stage’ ovary in older animals characterized by mainly interstitial tissue interspersed with a few degenerative follicles and cords of epithelial tissue. There is an overall decrease size and weight of the organ. There can be interstitial cell hyperplasia.

**Tubulostromal adenoma**: usually unilateral mass of dilated tubules lined by non-ciliated cuboidal epithelium with alveolar and/or tubule structures that can have narrow lumens. These structures are separated by various sized large round to polygonal cells that can resemble stromal interstitial cells, which may have brown pigment or foamy cytoplasm.