**Figure Legend:**

- **Figure 1** Normal skin in a male B6C3F1 mouse from a subchronic study.
- **Figure 2** Epithelial hyperplasia—increased numbers of squamous cells in the epidermis (arrow) and follicular epithelium (arrowheads) in a female B6C3F1 mouse from a subchronic study.
- **Figure 3** Sebaceous gland hyperplasia—increased numbers of sebocytes forming lobules around central ducts in a male F344/N rat from a subchronic study. **Figure 4** Sebaceous gland hyperplasia—increased numbers of sebocytes forming lobules around central ducts in a male F344/N rat from a subchronic study. **Figure 5** Follicular hyperplasia—increased numbers of follicular units within the dermis and subcutis in a female B6C3F1 mouse from a subchronic study.

**Comment:** *Epithelial hyperplasia* is the most common spontaneous, non-neoplastic lesion of the skin observed in B6C3F1 mice in NTP studies. Hyperplasia of the epithelium of the epidermis and adnexa is also a common response to dermal application of chemicals. In more severe cases, especially when accompanied by inflammation, hyperplasia of follicular epithelium, follicular units, and sebaceous glands often occurs. It is characterized by increased thickness of the nonkeratinized layers of the epidermis due to an increased number (layers) of epithelial cells (Figure 2) compared with the same site in a control animal (Figure 1). The epithelium of the hair follicles may also be affected. This increased thickness may involve all three nonkeratinized layers (basal, spinous, and granular) but may be most apparent in the spinous cell layer. In more severe cases, the follicular epithelium may also be hyperplastic (Figure 2). This lesion can result after a wide variety of injuries and conditions, including spontaneous and experimentally induced inflammatory processes, exposure to irritants or toxic materials, repeated abrasion of the superficial keratin layer, and prolonged exposure to ultraviolet light.

*Sebaceous gland hyperplasia* is characterized by large sebaceous glands with increased numbers of cells forming numerous lobules around central ducts (Figure 3 and Figure 4). Over the period of a 2-year study, sebaceous hyperplasia has the potential to progress to benign and malignant sebaceous cell neoplasms.
Follicular hyperplasia is characterized by increased numbers of follicular units within the dermis and subcutis (Figure 5). Follicular epithelial hyperplasia is characterized by increased numbers of follicular epithelial cells within the hair follicles; it is typically an extension of epithelial hyperplasia of the epidermis but may be seen in the absence of epidermal hyperplasia.

Recommendation: “Epithelial hyperplasia” is preferred over the term “acanthosis.” Whenever present, epithelial hyperplasia should be diagnosed and assigned a severity grade. When follicular epithelium is also hyperplastic, this should be reflected in the severity grade assigned to epithelial hyperplasia and described in the pathology narrative. If follicular epithelial hyperplasia occurs without epidermal involvement, the term “Skin, Hair follicle, Epithelium – Hyperplasia” should be used. Associated lesions, such as inflammation, should be diagnosed separately. When present as a regenerative response, secondary to an adjacent ulcer, hyperplasia should not be diagnosed but should be described in the narrative.

When present, sebaceous hyperplasia or follicular hyperplasia should be diagnosed and assigned a severity grade. Hyperplasia of the sebaceous cells is often accompanied by hypertrophy. In such cases, hypertrophy need not be diagnosed.

References:


Authors:

Molly H. Boyle, DVM, MPH, DACVP
Toxicologic Pathologist
Integrated Laboratory System, Inc.
Research Triangle Park, NC

Georgette D. Hill, D.V.M., Ph.D.
Toxicologic Pathologist
Assistant Pathology Program Manager
Integrated Laboratory Systems, Inc.
Research Triangle Park, NC