Lung – Regeneration

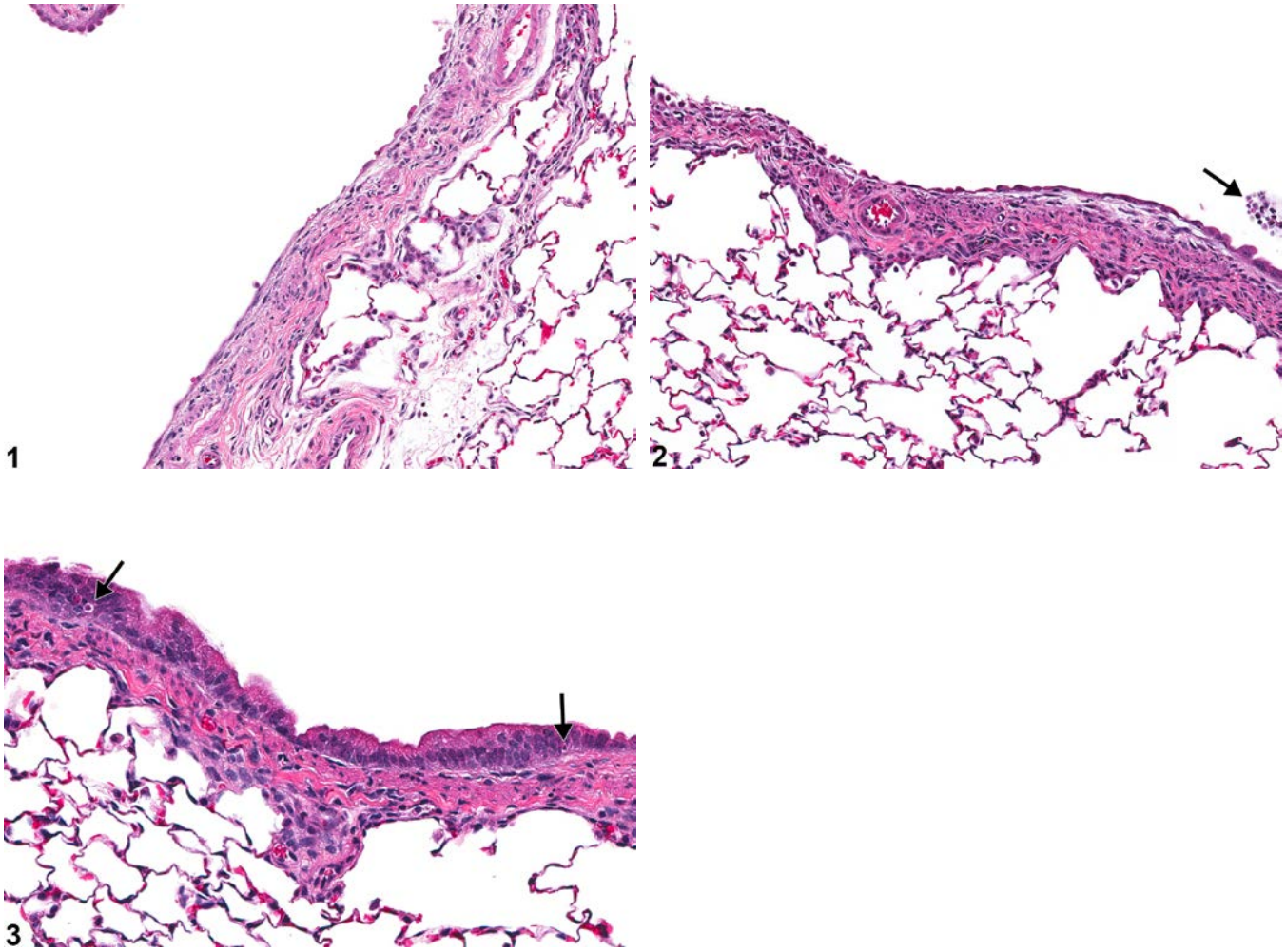
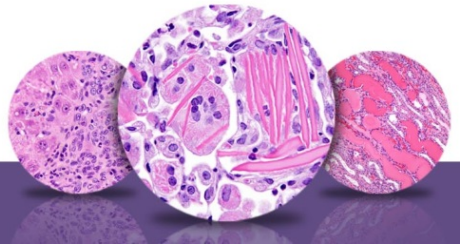


Figure Legend: **Figure 1** Lung, Bronchiole - Regeneration in a male Wistar Han rat from an acute study. A single, thin layer of flattened epithelial cells covers the bronchiolar surface. **Figure 2** Lung, Bronchiole - Regeneration in a male Wistar Han rat from an acute study. There is a single layer of flattened epithelial cells on the bronchiolar surface; the cell debris (arrow) in the bronchiolar lumen suggests epithelial damage. **Figure 3** Lung, Bronchiole - Regeneration in a male Wistar Han rat from an acute study. The scattered necrotic cells in the epithelium (arrows) suggest that this hyperplastic response is associated with regeneration secondary to previous damage.

Comment: Regeneration is the process whereby denuded portions of epithelium-lined surfaces (i.e., airways and alveoli) are repaired. Once the epithelium becomes necrotic or ulcerated, the adjacent,



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viable epithelial cells replace the lost cells. In the airways, the process begins with elongation of the adjacent epithelial cells, which become flattened, and migration of these cells across the wound to cover the basement membrane (Figure 1 and Figure 2). In later stages, the epithelium begins to proliferate to replace the lost cells to return the epithelial lining to its normal state. In the alveoli, the type II pneumocytes are the progenitor cells and undergo these processes to replace lost alveolar type I cells. In some cases, the regenerating epithelium may overshoot the normal number of epithelial cells and become hyperplastic (Figure 3). In such cases, in the absence of recognizable necrosis or ulceration, it may be difficult to determine whether the hyperplasia is due to regeneration or is a primary response to test article exposure. For this reason, the term “regeneration” is reserved for those cases where there is evidence of epithelial damage. Other features of regeneration may include characteristics consistent with cellular proliferation, such as karyomegaly and cytomegaly. Additionally, the proliferating cells may have a slightly atypical appearance, so the pathologist may need to distinguish between regeneration and cellular atypia.

Recommendation: Lung - Regeneration should be diagnosed whenever present and evidence of necrosis or degeneration is also present. If the number of epithelial cells exceeds that which would be considered within normal limits, hyperplasia should be diagnosed, regardless of whether it is a direct effect of test article exposure or excessive regeneration, but the pathogenesis of the hyperplasia should be discussed in the pathology narrative. A site modifier (e.g., bronchus, bronchiole, alveolus) should be included in the diagnosis to indicate the location of the lesion. Regeneration should not be graded. To convey the severity of the lesion, either necrosis or degeneration must be diagnosed concurrently and graded (see Lung, Epithelium - Degeneration and Lung, Epithelium - Necrosis). Other associated lesions, such as inflammation, should be diagnosed separately. If the pathologist judges that the regenerating epithelium exhibits significant features of atypia, then Lung - Atypia, Cellular should be diagnosed and graded.

References:

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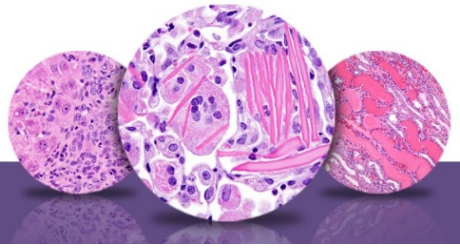

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Authors:

Mark F. Cesta, DVM, PhD, DACVP
Staff Scientist/NTP Pathologist
NTP Pathology Group
National Toxicology Program
National Institute of Environmental Health Sciences
Research Triangle Park, NC

Darlene Dixon, DVM, PhD, DACVP
Group Leader
Molecular Pathogenesis Group
National Toxicology Program
National Institute of Environmental Health Sciences
Research Triangle Park, NC

Ronald A. Herbert, DVM, PhD
Group Leader/NTP Pathologist
Pathology Support Group
National Toxicology Program
National Institute of Environmental Health Sciences
Research Triangle Park, NC

Lauren M. Staska, DVM, PhD, DACVP
Senior Pathologist
WIL Research
Hillsborough, NC