Question 1:

The imiquimod (IMQ) model used to study human psoriasis is what type of murine model?

● Acute (inducible) model

Explanation:

The IMQ-induced psoriasiform-like dermatitis system is considered an acute murine model. In this system, 5% topical IMQ is applied daily to the backs or ears of mice for approximately 1-2 weeks. IMQ acts primarily through the activation of Toll-like receptor 7/8 and results in acute skin inflammation (e.g. redness, scaling, and epidermal thickening/induration) within 2-3 days. Skin inflammation worsens with continued application. Importantly, the IMQ model cannot be used to study the chronic effects of skin inflammation in mice since topical application with this agent for more than 2 weeks results in severe dehydration and death.

❍ Whole-body transgenic model

❍ Tissue-specific knockout

❍ Xenograft model

Question 2:

Which is a primary limitation of the IMQ-induced model used to study human psoriasis?

❍ The need for long-term topical application to induce an inflammatory skin phenotype

❍ The significant technical expertise required to use this model system

● The non-specific nature of the skin inflammation induced by topical IMQ

Explanation:

The primary limitation of the IMQ-induced mouse model is the relatively non-specific nature of skin inflammation induced by this chemical. As a result, the IMQ-induced model along with other acute model systems, such as 12-O-tetradecanoylphorbol-13-acetate (TPA) and oxazolone, have been used to simultaneously support research findings for multiple distinct skin diseases (e.g. psoriasis, atopic dermatitis, and allergic/irritant dermatitis). Advantages of the IMQ-induced model system include its convenience, relative ease of use, and ability to rapidly induce a skin phenotype in multiple genetic strains of mice.

❍ The ability of IMQ to induce skin inflammation in a single genetic strain of mice

Question 3:

Compared to whole-body transgenic mice, what is one advantage of a tissue-specific transgenic mouse model?

❍ Tissue-specific transgenic models are not associated with embryonic or early prenatal death

❍ Tissue-specific transgenic models are less inexpensive and are not labor-intensive

❍ Tissue-specific transgenic models overcome the potential for undesirable/leaky gene expression

● Tissue-specific transgenic models enable scientists to isolate the molecular mechanisms directly contributing to an observed phenotype

Explanation:

In contrast to traditional whole-body transgenic mice, tissue-specific transgenic mouse models limit gene alterations (i.e. increased or decreased/absent expression) to certain cell populations or tissue types under the regulation of a particular gene promoter. For example, the use of a keratin-5 promoter restricts the expression of a gene to cell types that express keratin-5, such as epithelial keratinocytes. This allows scientists to determine how the over-expression or absence of a gene in a specific tissue or cell type impacts an observed phenotype in the studied mice. Tissue-specific transgenic mice are expensive, labor-intensive, can be associated with embryonic or early prenatal death, and have potential for undesirable or “leaky” gene expression.

Question 4:

Which type of mouse model is felt to most closely mimic the cellular, phenotypic, and genetic characteristics of human disease?

❍ Acute (inducible) model

❍ Whole-body transgenic model

❍ Tissue-specific knockout

● Xenograft model

Explanation:

The xenograft or “humanized” mouse models of psoriasis are created by the transplantation of human psoriasis skin or immune cells onto severely immunocompromised mice (e.g. SCID or AGR129 genetic strains). The primary advantage of this mouse model type is that it enables scientists to directly study transplanted psoriatic tissues grown in murine hosts that lack T and B lymphocytes. The phenotypes of xenotransplantation psoriasis models best recapitulate the human disease since they are primarily dependent on the inherent cellular, immune, and genetic characteristics of the transplanted donor tissues. However, xenograft models are the least commonly used model type due to the technical challenges associated with tissue transplantation, the requirement for large amounts of human tissue, and substantial phenotype variations observed between donors.

Question 5:

Which of the following factors are potential confounding variables that may affect the interpretation of an inflammatory phenotype in a psoriasis-like mouse model?

❍ Gestational age or gender of the mice

❍ The vehicle of topical applications

❍ Alterations in the murine microbiome

● All of the above

Explanation:

The are many experimental variables which may alter an observed phenotype in experimental mouse models. Examples of confounding variables include gestational age, gender, diet, genetic strain of the mouse model, housing conditions, unintended consequences of the treatment vehicle or preservatives contained in medications, and alterations in the murine microbiome. Controlling for all of these confounding variables can be very difficult and requires carefully designed experiments and the use of multiple controls.