Define “Humanized”: Two Mouse Models Helping Produce Cancer Immunotherapies

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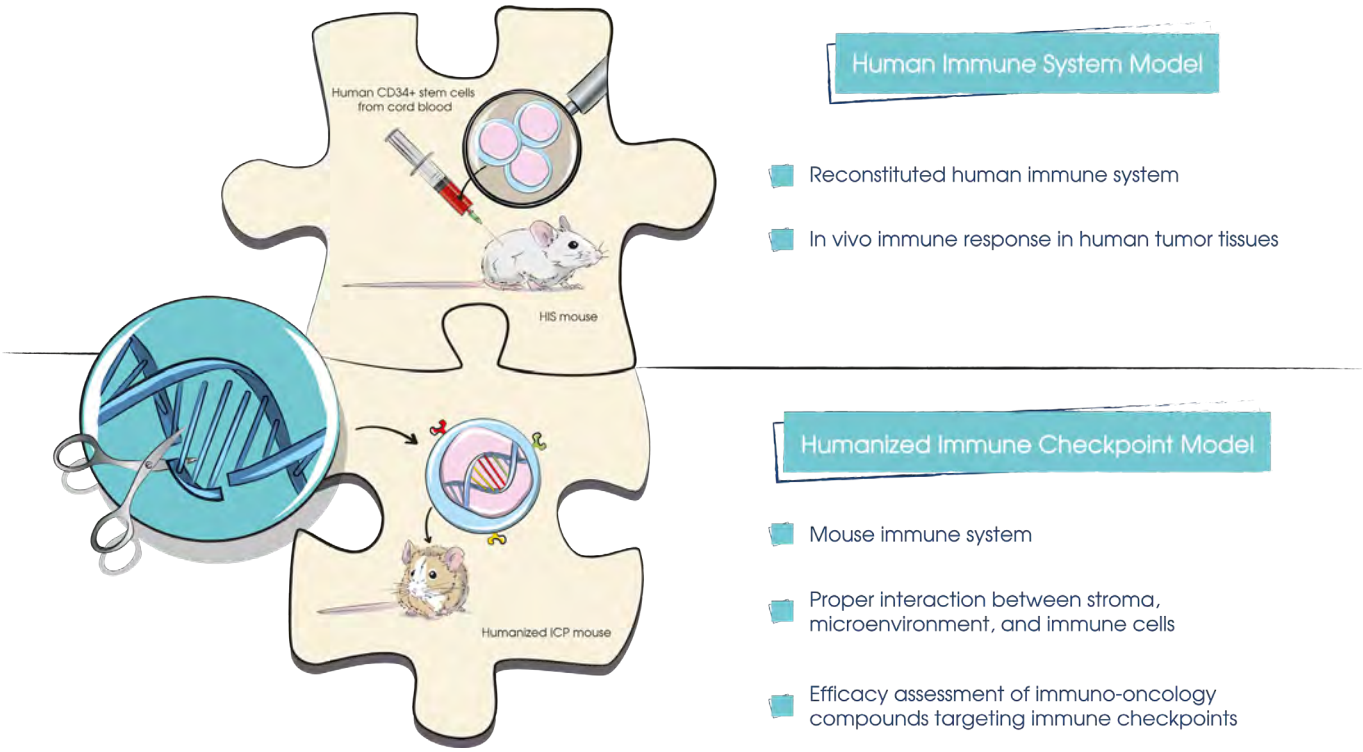
Official numbers say that we are winning our war on cancer: mortality rates corrected for aging have fallen by 17% from 1990 to 2016 and are still declining. Some say cancer prevalence is decreasing because of earlier detection, others because of improved treatment.[1] What is certain is that recent decades have seen a significant boost of immunotherapeutic approaches that have dramatically contributed to improved survival rates for several cancer types. For example, patients suffering from some solid cancers and hematological malignancies, whose outcomes were once invariably terminal, can now be treated with immunotherapy drugs (e.g., ipilimumab, nivolumab) or CAR T-cell therapy, and experience durable remissions.[2,3]

These important advances are mainly due to the generation of sophisticated preclinical models that translate better to the human situation, and therefore help scientists to improve the design of clinical trials in cancer immunotherapy. Among those are human immune system (HIS) and humanized immune checkpoint (ICP) mice.[4-6]



Although both models are humanized, each is done differently. HIS are immunocompromised mice reconstituted with human cellular and molecular components to develop a human immune system: when engrafted with tumors of human origins, they represent invaluable tools to study and predict therapy-induced immune responses *in vivo*.[6-8]

Humanized ICP models are genetically modified by Knockin at specific loci, resulting in the replacement of the murine protein with the human counterpart. As such, they preserve the target-ligand interaction as well as the molecular and cellular communication between stromal and cancer cells. For this reason, especially when injected with humanized ICP tumor cell lines originating from the very same genetic background (i.e., syngeneic models), humanized ICP mice provide important insights into the process of metastasis, and into the efficacy of mono and combination therapies targeting human ICPs.[9]

HIS and ICP mice are therefore complementary models as, when used together, they allow not only to assess the efficacy and safety of immunotherapies, but also to determine the immune response elicited by the treatment.

Please follow these links if you wish to read more on:
Preclinical models in immuno-oncology: https://www.genoway.com/commentaries/immuno-oncolology-models.htm
Mice reconstituted with a human immune system (HIS): https://www.genoway.com/commentaries/brgsf-his.htm
Humanized Immune Checkpoint mouse models: https://www.genoway.com/commentaries/icp.htm
Syngeneic mouse models: https://www.genoway.com/model-use/onco/syngeneic-model.htm

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