

# Myeloproliferative Neoplasm Animal Models

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## KEYWORDS

- Myeloproliferative neoplasms • Preclinical murine models • BCR-ABL • JAK2V617F
- Hematopoietic stem cells • Bone marrow microenvironment • Myelofibrosis
- Oncogenes

## KEY POINTS

- Retroviral transduction of *BCR-ABL* into murine bone marrow cells followed by transplantation into irradiated syngeneic mice established the field of myeloproliferative neoplasm (MPN) animal modeling.
- The effects of the *JAK2V617F* mutation in hematopoietic cells has been extensively modeled in vivo using retroviral, transgenic, knock-in, and xenograft murine models.
- The considerable phenotypic differences observed between broadly similar *JAK2V617F* murine models highlights the inherent variability in murine models that can occur as a result of multiple factors, such as promoter, oncogene expression level, murine versus human protein, and mouse strain.
- Mutant oncogenes found in human acute myelogenous leukemia (AML), such as *RAS* and *FLT3*, induce MPNs in mice, indicating that these genetic lesions are insufficient to cause AML and suggesting that additional cooperating genetic events are required for AML development.
- As the increasing genetic complexity of MPNs has become apparent, additional genetic models have been developed to investigate the functional effects and therapeutic susceptibilities of compound genetic lesions in MPNs.

## INTRODUCTION

Animal models have been used extensively in the study of myeloproliferative neoplasms (MPNs) and have played a key role in advancing the biologic understanding of these diseases (**Boxes 1–3**). In general, these models have faithfully recapitulated human MPNs in mice, enabled detailed characterization of the effects of specific MPN-associated genetic abnormalities on the hematopoietic stem and progenitor

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