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Introduction

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A set of seminal observations, in 2002 and 2003, has ignited major interest in the science and practice of eosinophilic disorders and systemic mastocytosis (SM) [1–4]. It all started with the clinical observation that imatinib mesylate produced impressive responses in both 'hypereosinophilic syndrome (HES)' [1] and SM [2], in the absence of the *bcr/abl* oncoprotein. This was followed by the discovery of the specific drug target in both instances, FIP1L1-PDGFRA [3]. A large clinical study has subsequently demonstrated that the dramatic treatment responses to low-dose imatinib mesylate (100 mg/day) occurred only in the presence of the *FIP1L1-PDGFRA* mutation, and that the phenotype that was linked to the particular genotype was SM associated with prominent blood eosinophilia (SM-eos) [5]. Also in 2002, imatinib mesylate was shown to be effective in a related, eosinophilia-associated myeloproliferative disorder that was characterized by a mutation in the other PDGFR gene, *PDGFRB* [4]. The latter appeared to be always associated with a microscopically detectable cytogenetic lesion involving chromosome 5q33 [6], while *FIP1L1-PDGFRA* is cytogenetically occult [3].

The above-mentioned developments have led to the reclassification of both eosinophilic disorders and SM into treatment-relevant categories [7, 8]. In this regard, it is important to note that imatinib mesylate is ineffective, both in vitro and in vivo, against D816V *c-kit*-mutated SM as well as the majority of patients with true HES [5, 9, 10]. In the former instance, it is hoped that the problem will be overcome by the therapeutic utilization of second-generation kinase inhibitors that have shown in vitro activity against D816V *c-kit*-mutated cell lines [11, 12]. These and other similarly acting drugs [11, 13] might also show enhanced therapeutic activity in molecularly undefined HES. Another drug that has been shown to have excellent clinical activity in SM is cladribine, although the mechanism of action has not been well delineated [14–16]. Despite the aforementioned major advances, much remains to be discovered in terms of both pathogenesis and treatment of SM and HES. In the current mini-symposium, my colleagues and I have summarized the current state of knowledge in the biology, classification, and treatment of primary eosinophilic disorders, including HES and SM.

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