With great interest we read the recent report ‘Chronic lymphocytic leukemia and myeloproliferative neoplasms concurrently diagnosed: clinical and biological characteristics’ by Todisco et al. describing a cohort of patients with coinciding diagnoses of chronic lymphocytic leukemia (CLL) and myeloproliferative neoplasms (MPN) in their center. The overall incidence of 13 patients with concomitant CLL in a cohort of 1719 PMN patients was noted to be higher than to be expected from the incidence of CLL in the general population. They found two patients with polycythemia vera (PV) and CLL. This lead the authors to speculate on a possible common pathophysiological basis for the occurrence of both a myeloid and lymphoid neoplastic clone in these patients.[1]

Although we agree that the incidence of CLL observed in this MPN cohort is considerably higher than would be expected based on a calculated rate of coincidental occurrence, we wondered if a detection bias may confound the comparison with the general population. As CLL is present asymptomatically in the majority of patients, the prevalence is likely to be underestimated in the general population. This is apparent from other cohort studies of thoroughly medically screened subjects [2] and may explain the higher incidence of monoclonal B-cell lymphocytosis (MBL) in patients with MPN.[3] Asymptomatic CLL patients thus have a higher chance of detection of their CLL clone in case of a concomitant MPN diagnosis due to the investigations of peripheral blood and bone marrow they are generally subjected to.

For comparison, we investigated the prevalence of concomitant myeloid malignancies in a retrospective cohort of 155 patients with PV from ten nonacademic teaching hospitals in the Netherlands we recently reviewed. We found one patient with a concomitant diagnosis of CLL, one patient with MBL and one patient with chronic myelomonocytic leukemia. The CLL patient in our cohort study was a 72-year-old female with JAK2 V617F positive PV in whom the diagnosis of CLL was made based on the routine immune fluorescence panel of both blood and bone marrow obtained in the context of investigations for her suspected PV at the time of diagnosis, prior to initiation of treatment. She had an asymptomatic Rai 0, Binet A stage CLL. Interestingly, there was a clear positive family history for PV in our patient as she had two relatives who were also diagnosed with PV.

Secondly, we performed a chart review of all CLL patients diagnosed between 2000 and 2015 in our center. In the 374 CLL patients thereby identified, there were two patients with a concomitant MPN. One patient was the case from the PV cohort described above. However, there was a second case of a patient presenting with a combined diagnosis of CLL and MPL W515L mutation positive primary myelofibrosis.

Our cases may be perceived as examples of detection bias. However, the consistency with which coincidental occurrences are observed in the various cohorts makes this less likely as CLL and MPN by themselves have a very low incidence. Also, the positive family history in our PV patient provides an important clue for an underlying genetic aberrancy predisposing to the development of mutations driving either myeloid or lymphoid clonal proliferation. Indeed, Todisco et al. also found a very high incidence (23%) of a positive family history in their MPN patients with CLL.[1]

Taken together, we believe that although incidence rates of concomitant hematological...
malignancies may be skewed by detection bias, the observations of familial clustering in the cases presented by Todisco et al. and in the patient from our additional cohort provide substance for the hypothesis that there may be germline genetic mutations predisposing to the development of clonal diseases of diverse lineage.

Potential conflict of interest: The results of the retrospective cohort of 155 PV patients were based on a Novartis sponsored chart review. Disclosure forms provided by the authors are available with the full text of this article online at http://dx.doi.org/10.1080/10428194.2016.1260123.

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