Reviewer's report

Title: SPARC expression in CML is associated to imatinib treatment and to inhibition of leukemia cell proliferation

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Reviewer: osvaldo podhajcer

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The aim of the work by Giallongo et al was to assess SPARC levels produced by blood cells from CML patients before and after imatinib (IM) treatment. Authors aimed to identify cells responsible for SPARC production. They found that SPARC levels increased for several months in blood after IM treatment and the main source of SPARC are normal cells and mainly monocytes. Importantly, they found that SPARC synergized with IM to inhibit the K562 myeloid cells growth.

Changes in SPARC levels produced by PBMC are clearly shown as the correlation between IM treatment and SPARC levels. They also clearly shown that the granulocyte population after IM treatment is not a cancerous one. The combined effect of IM and SPARC on K562 cell survival and arrest is also clear although not very impressive.

I think the work is of value for the field in particular due to the previous evidence by Fenouille et al (2010) where they showed that K562 cells resistance to IM involves SPARC and the fyn-erk intracellular pathway. Fenouille et al also showed increased expression of SPARC in patients that developed resistance to IM treatment. They proposed that the fact that SPARC is not released by CML cells could be associated with its involvement in IM resistance.

However the present data shows that in fact SPARC might work in combination with IM to induce CML cells arrest. It can be hypothesized that SPARC secreted by normal non-CML cells can synergize with IM in vivo.

I would recommend the authors to perform additional experiments

a) cells treatment with IM in the presence of SPARC antibodies to establish whether SPARC might mediate IM effect.

b) Additional studies of interest include to evaluate the effect of IM with or without SPARC in IM-resistant CML cells

c) An interesting study could be to take serum before and after IM treatment to treat K562 cells in vitro in the presence or not of IM. The serum before IM treatment should have no anti-K562 effect while the contrary should happen with the post IM-treatment serum. A SPARC antibody would confirm that this a SPARC mediated effect.

Minor

a) The word SPARC is lacking in the title
b) The growth inhibitory and antiangiogenic role of SPARC also depends on the cell type as the pro or antitumorigenic role (first paragraph of the abstract).

c) In pancreatic cancer SPARC expression by stromal fibroblasts is associated with poorer prognosis (Infante, 2007)

d) In Figure 1 it must be mentioned that data are referred to levels found in healthy controls

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests