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Data Article

Sensitivity to imatinib of KCL22 chronic myeloid leukemia cell survival/growth and stem cell potential under glucose shortage

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ABSTRACT

The data presented here are related to the original research article entitled "Imatinib enhances the maintenance of Chronic Myeloid Leukemia (CML) stem cell potential in the absence of glucose" (Bono et al., 2018). The sensitivity to the tyrosine kinase inhibitor imatinib-mesylate (IM) of KCL22 CML cells cultured under glucose shortage have been determined by scoring cell survival/growth via trypan blue exclusion and stem cell potential via Culture Repopulation Ability (CRA) assay. Discussion of the data can be found in Bono et al. (2018).

Specifications table

Subject area	*Biology*
More specific subject area	*Cell biology*
Type of data	*Graph*
How data was acquired	*Count of viable cells; Culture Repopulation Ability (CRA) assay*
Data format	*Analyzed*

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Experimental factors	*KCL22 CML cells cultured in the presence or absence of imatinib under glucose shortage*
Experimental features	*Measure of cell survival/growth; measure of stem cell potential*
Data source location	*Florence, Italy*
Data accessibility	*All data are shown within this article*

Value of the data

- Data provide a proof of concept that the treatment with IM may be detrimental to a favorable outcome of CML, via the enhancement of CML stem cell potential.
- Data support via the use of a different CML cell line, namely KCL22 cells, the results obtained with K562 cells [1].

1. Data

CML is a hematopoietic disease driven by the oncogenic BCR/Abl protein, a constitutively active tyrosine kinase, therapeutically targeted by the tyrosine kinase inhibitor (TKI) imatinib-mesylate (IM). IM is extremely efficient in ensuring remission of disease but not in preventing the risk of relapse upon withdrawal of therapy. This is most likely due to the refractoriness to TKI of leukemia stem cells (LSC) enriched under energy restriction (oxygen and/or glucose shortage). We previously demonstrated that IM enhances the maintenance of CML K562 stem cell potential in the absence of glucose [1]. Here, we extend these findings to another CML cell line, KCL22 cells, thus corroborating the proof of concept obtained with K562 cells.

The effects of IM on KCL22 cell growth under glucose shortage are shown in Fig. 1A. Viable cell number underwent a 3-fold increase, peaking on day 6, to decline thereafter, as expected, due to nutrient consumption. IM addition on day 2 determined irrelevant effects until day 3, to suppress thereafter cell growth completely. Such an outcome is in keeping with the presence of BCR/Abl protein, the molecular target of IM, on day 2 of incubation of KCL22 cells under glucose shortage (Fig. 1B and [2]). The effects of glucose shortage and IM treatment on the maintenance of KCL22 CML stem cell potential in culture were then tested by Culture Repopulation Ability (CRA) assay (Fig. 1C).

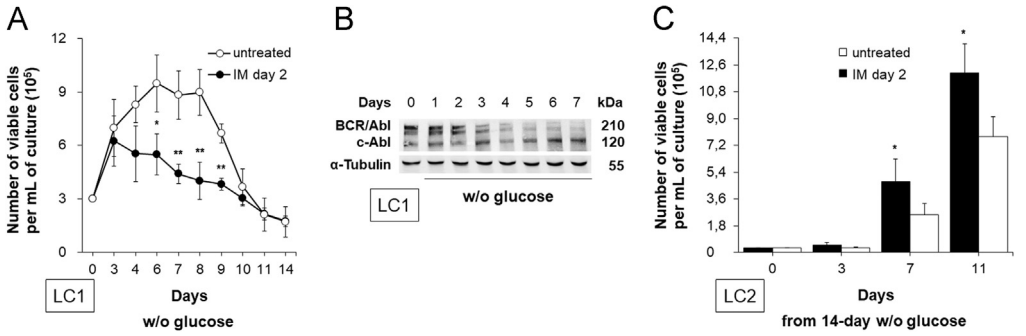

Fig. 1. Effects of IM on KCL22 cell growth and stem cell potential in the absence of glucose. (A) KCL22 cells were plated at 3×10^5 cells/mL in glucose-free medium (LC1) and incubated for the indicated times: (o) untreated control; (●) IM administered on day 2. Viable cells were counted by trypan blue exclusion. Data represent the mean ± SD of 3 independent experiments. * $p < 0.05$ day 6, ** $p < 0.01$ from day 7 to day 9 (two-tailed Student's *t* test). (B) The levels of BCR/Abl protein in cells incubated like in (A) were determined by Western blotting using α-Tubulin as loading control. (C) KCL22 cells were cultured and treated or not with IM (LC1) like in (A). On day 14 of incubation in LC1, cells were washed free of drug and replated (3×10^4/mL) into IM-free secondary liquid cultures (LC2) supplemented with standard glucose concentration. The maintenance of stem cell potential at the end of LC1 was determined by counting viable cells (trypan blue exclusion) at the indicated times of incubation in LC2. Data represent the mean + SD of 3 independent experiments. * $p < 0.05$ from day 7 (two-tailed Student's *t* test).

KCL22 cells from cultures established in the absence of glucose and treated with IM on day 2 (Liquid Culture 1 -LC1-, shown in A) were transferred on day 14 to non-selective (standard glucose concentration, no IM) secondary liquid cultures (LC2), to exploit therein their repopulation potential (C). As expected, LC1 cells did not induce culture repopulation during the early days of incubation in LC2 [3,4]. Starting from day 7 of LC2, IM-treated LC1 cells showed increased repopulation ability compared to untreated cells, indicating that IM protected stem cell potential from its suppression in glucose-free cultures.

2. Experimental design, materials and methods

2.1. Cells and culture conditions

KCL22 blast-crisis CML cells were obtained from the German Collection of Cell Cultures (Braunschweig, Germany) and cultured as described [2]. The experiments were carried out using RPMI 1640 medium without D-glucose (Gibco by Thermo Fisher Scientific, Waltham, MA, USA). IM was dissolved in PBS (EuroClone) and IM-untreated cultures were PBS-supplemented. Experiments were established (3×10^5/mL) with exponentially-growing cells. Viable cells were counted in a hemocytometer by trypan blue exclusion.

2.2. Culture Repopulation Ability (CRA) assay

The CRA assay is an in vitro assay that estimates the stem cell potential via cell transfer to liquid cultures (LC2), instead of transplantation into syngeneic animals like in the cognate Marrow Repopulation Ability assay in vivo [4–10]. Cells from cultures where the experimental variants are applied (LC1), at the 14^{th} day of incubation in LC1 were washed free of IM and replated (3×10^4 cells/mL) into IM-free LC2 containing standard glucose concentration. Culture medium was never changed during LC1 or LC2. The kinetics of viable cell number in LC2 provides an estimate of the CRA of LC1 cells.

2.3. Cell protein content analysis

Cells were washed once with ice-cold phosphate buffered saline (PBS) containing 100 μM Na_3VO_4. Total cell lysates were obtained in Laemmli buffer (62.5 mM Tris/HCl, pH 6.8, 10% glycerol, 0.005% bromophenol blue, and 2% SDS). Protein concentration was determined by the BCA method (#23225, Pierce™ BCA Protein Assay Kit by Thermo Fisher Scientific) and 50 μg protein/sample were subjected to SDS-PAGE as described [1]. Antibodies used for Western blotting were: anti-c-Abl (K-12), rabbit polyclonal (#sc-131, Santa Cruz Biotechnology, Santa Cruz, CA, USA), anti-α-Tubulin (clone DM1A), mouse monoclonal (#T9026, Sigma-Aldrich, St. Louis, MO, U.S.A.), IRDye®800CW- or IRDye®680-conjugated secondary antibody (LI-COR® Biosciences, Lincoln, NE, U.S.A.) [11]. Antibody-coated protein bands were visualized by the Odyssey Infrared Imaging System (LI-COR® Biosciences) [12].

2.4. Statistical analysis

Data are presented as mean ± SD (unless specified otherwise) of the indicated number of independent experiments and were compared by using the Student's t test; p values ≤ 0.05 were considered statistically significant.

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Transparency document. Supporting information

Transparency data associated with this article can be found in the online version at https://doi.org/10.1016/j.dib.2018.09.041.

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