Guidelines for contributors to conference proceedings

These instructions are designed to assist contributors in preparing typescripts for publication in Royal Society of Chemistry **conference proceedings**. Please read them very carefully and follow the specifications they contain. There is a **sample chapter** at the end, which illustrates how the finished chapter should look. A simple **template** is also available. Chapters will be published as they are submitted to us and will not be edited or re-formatted, so it is essential that the guidelines below are followed. You **will not** receive a proof of your submission prior to printing.

Contents

1 Submission of typescripts

The final typescript should be **emailed to the Editor** of the book, and should be submitted as a Word file. We cannot accept PDFs. You must also supply the editor with your signed **Licence to Publish** form. **We cannot proceed with production without this.**

2 Preparation of typescripts

A simple **template** document has been created to assist in the preparation. Settings within the template have already been fixed in accordance with the specifications given here so that the correct layout and style of material is produced. Alternatively, if not using the template, document settings should follow the guidelines below.

Abstracts – Every chapter must be accompanied by an abstract. The abstracts should be provided in a separate file and not part of the chapter. We will be using the abstracts in our eBook collection to promote the content; they will not appear in the printed book. The abstract should be a 50–250 word summary of the work and must not include references or figures.

Page layout – Paper size: *Custom*, 15.6 cm wide × 23.4 cm high. **Margins**; *top*: 2.3 cm, *bottom, left and right*: 1.7 cm. **Font**: Arial 10pt. The text should be **justified** and occupy the whole page. **Single** line spacing should be used.
Do not leave pages short of the bottom margin. If there is insufficient space for a figure or table at the bottom of a page, complete the page with subsequent text and place the figure or table at the top of the next page.

Chapter title and contributors' details – The chapter title and the names and addresses of the contributors should appear at the top of the page as shown in the sample chapter. The chapter title should be in all **upper case** and start on line 1. The contributors' names should start on line 8. There should be one line space following the contributors' names before the addresses. The first main heading should start on line 18.

Headings – Headings and sub-headings should be typed in the styles below. Headings should not be the last line on a page.

1 MAIN HEADING

Main headings should be flush left, numbered with Arabic numerals followed by a single space and then the heading typed all in upper case. There should be one line of space above it and one below it. The first line of text following the heading should be flush left.

1.1 First-value sub-heading

First-value sub-headings are typed flush left with initial capitals for principle words, double-numbered, *ie* 1.1, 1.2 *etc* and bold. There should be one line space above and one line below.

1.1.1 Second-value sub-headings. Second-value sub-headings are typed as part of the succeeding paragraph with initial capitals for all principle words, double-numbered, and italic. They are followed by a full stop and the text begins on the same line. One line space should be left above the heading.

Paragraphs – The first line of each paragraph should be indented 0.5 cm except when following a heading (when it should be flush left). A line should not be left between paragraphs.

3 Presentation of material

Figures – All figures must be supplied **greyscale**. Graphs *etc.* should be embedded as images rather than editable objects. Figures should be positioned on the same page as the text in which they are discussed or on the following page. They are best positioned **centrally at the top or bottom** of a page. If the figure is not at the top of a page there should be one line space above it. All illustrations should be mentioned in the text.

Each figure should have a descriptive caption, numbered in a single sequence beginning **Figure 1**, **Figure 2**, *etc*. The rest of the caption should immediately follow on and be typed in italics and placed **below** the figure. There should be a full point at the end of the caption. There should be a line space above and below the caption.

Electronic artwork files should be of adequate resolution; **300–600dpi** is recommended. If figures are being reproduced from another publication, please ensure you have obtained and acknowledged **copyright permission**. For further information about this, please see the document: **Copyright information and permissions form**. The completed form should be returned with your chapter to your editor if applicable.

Equations – These should be flush left and displayed on a separate line with a line space above and below them. The equations should be numbered in a single sequence using Arabic numerals in parentheses on the right-hand side of the page.

Tables – These should be placed at the top or bottom of a page and be centred on the page width. Each table should have a descriptive caption **above** the table, beginning **Table 1**, **Table 2** *etc*. The rest of the caption should immediately follow on and be typed in italics. There should be a full point at the end of the caption. There should be one line space above and below the caption. Table border lines should only appear above and below the table header row and at the foot of the table.

Bibliographic references and footnotes – References should be indicated in the typescript by superior Arabic numerals, which must be cited in numerical sequence and appear after any punctuation.

The abbreviations to be used for journal titles should follow the Chemical Abstracts Service Source Index (CASSI). The references should be collected at the end of the chapter, and do not need to be started on a new page. The style of references should follow the examples below. Pay particular attention to the use of punctuation and bold/italic fonts. An Endnote style file is available.

1. D. O. Bassett and A. J. Hills, *Am. Lab.*, 1987, **19**, 28.
2. E. Yourdon, *Modern Structured Analysis*, Yourdon Press, Englewood Cliffs, NJ, 1989.
3. A. W. Oxford in *Progress in Medicinal Chemistry*, ed. G. P. Ellis and D. K. Luscombe, Elsevier, Amsterdam, 1992, p. 239.

4 Sample chapter

The following pages illustrate most of the points made in the above sections.

DISCOVERY OF A SMALL, NON-PEPTIDYL MIMIC OF GRANULOCYTE COLONY-STIMULATING FACTOR

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1 INTRODUCTION

Granulocyte colony-stimulating factor (G-CSF) is a 21 kDa hematopoietic cytokine secreted by bone marrow stroma cells, macrophages, fibroblasts and endothelial cells. Recombinant human G-CSF, available in both glycosylated and non-glycosylated forms, has become an important therapeutic agent for the treatment of a variety of human neutropenias, including those resulting from chemotherapy, congenital defects and bone marrow transplantation.[1] Genetically engineered G-CSF, like any other recombinant growth factors, must be administered either subcutaneously or intravenously. Although other agents have been shown to activate cytokine receptors by oligomerization,[2] no smallmolecule cytokine mimics with potential for oral delivery have yet been reported.

2 METHOD AND RESULTS

2.1 Identification of a Suitable G-CSF Mimic

An assay was designed to identify non-peptidyl compounds that activate the G-CSF receptor based on activation of STATs, which are known to play a central role in the GCSF-mediated responses. From the drug resistant clones responsive to G-CSF, a single clone, which exhibited 20-fold induction of luciferase activity by G-CSF and the same pattern of JAK and STAT activation as the parental cells, was selected to screen a library of synthetic organic compounds. For the screen, the cells were incubated for 2.5 hours with individual compounds at a concentration of 10 μM in a 96 well plate format. Compound SB-247464 (Figure 1) was identified as a hit in the assay and showed a dose–response effect with a maximum efficacy of 30% that of G-CSF at 1 μM.

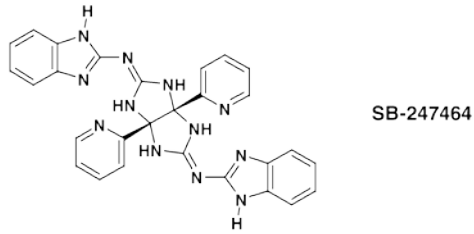

Figure 1 *Structure of SB-247464.*

As expected, SB-247464 induced activation of G-CSF signal transduction pathways, the efficacy being *ca.* 25–50% that of G-CSF, consistent with data from the luciferase assay.

2.2 Assessment of Activity of SB-247464

To assess SB-247464 in supporting the proliferation and differentiation of cells of the granulocytic lineage, colony-forming unit-granulocyte (CFU-G) assays from murine bone marrow were performed. SB-247464 stimulated the production of granulocytic colonies, with an efficacy 20–80% of that of G-CSF at 0.3–3 μM; the colonies appeared uniformly smaller than those promoted by G-CSF, but were consistently larger than 30 cells. Likewise, SB-247464 was able to mimic the activity of G-CSF *in vivo* (Figure 2): subcutaneous administration twice a day to normal mice caused a dose-dependent increase in peripheral blood neutrophils after 4 days. Efficacy at 30 mg/kg was comparable to that of 50 μg kg^{-1} of G-CSF, elevating the neutrophil counts to *ca.* 400% over baseline. The magnitude of the increase was equivalent to that effected by administration of 5–30 μg kg^{-1} day^{-1} of G-CSF to normal or neutropenic humans. Table 1 shows examples.

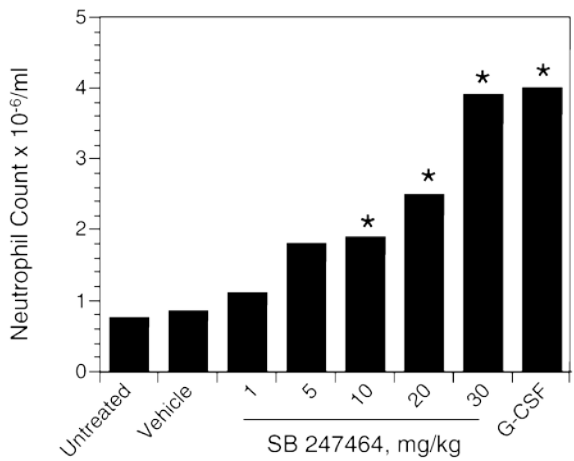

Figure 2 *Granulopoietic activity in vivo; ∗ indicate neutrophil counts.*

Table 1 *Neutrophil count and granulopoietic activity.*

Neutrophil count	*Granulopoietic activity*	*Data*
1	0.1	Yes
2	0.2	No
3	0.3	No
4	0.4	–
5	0.5	Yes

3 CONCLUSION

The identification of SB-247464 as a G-CSF mimetic provides proof of principle for drug discovery using JAK/STAT-based assays, and shows for the first time that a small nonpeptidyl molecule can trigger the selective activation of a cytokine receptor. These findings may lead to the development of orally available G-CSF mimics for use in the treatment of neutropenia.

References

1. K. Welte, J. Gabrilove, M.H. Bronchud, E. Platzer and G. Morstyn, *Blood*, 1996, **88**, 1907.
2. M. Fourcin, S. Chevalier, C. Guillet, O. Robledo, J. Froger, A. Pouplard-Barthelaix and H. Gascan, *J. Biol. Chem.*, 1996, **271**, 11756.