Reviewer's report

Title: Therapeutic effects of STAT3-decoy oligodeoxynucleotide on human lung cancer in xenograft

Version: 1 Date: 12 February 2007

Reviewer: Bart JL Eggen

Reviewer's report:

General
In this manuscript the authors investigated the therapeutic effect of a STAT3-decoy oligodeoxynucleotide on
the human non-small-cell-lung carcinoma cell line A549. They analyze the effect of this decoy both in vitro
and in vivo.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be
reached)

On page 12, the authors claim that they demonstrated in this study that STAT3 was constitutively activated
in several human lung cancer cell lines (data not shown).
This is not shown by the authors, they show that introduction of a STAT3-decoy oligodeoxynucleotide
resulted in reduced proliferation, induction of apoptosis, reduced tumor growth and reduced STAT3 target
gene expression. The evidence provided that inhibition of STAT3 activity is responsible for the effects
observed is circumstantial. It would make the manuscript stronger if the authors show that in these cells
STAT3 indeed is constitutively phosphorylated on Tyr705 and possibly also on Ser727. An alternative would
be to transfect these cells with a STAT3-responsive reporter construct in combination with increasing
amounts of the STAT3 decoy, to show progressive loss of STAT3-reporter activation.

The western blot presented in Figure 4, panel B does not support the conclusion that the decoy results in a
downregulation of Bcl-xl expression. There is no difference in Bcl-xl protein levels between the decoy oligo
and scrambled oligo treated cells.

Are the westerns and RT-PCR assays shown in Fig 4 performed on transfected cells purified by flow
cytometry or on whole cell populations? This is unclear from the manuscript and this information should be
included. If the latter is the case, how high was the transfection efficiency (%) and did that potneiutally lead
to an underestimation of the decoy effect.

The STAT3 targets c-myc and Survivin are not downregulated by treatment with the STAT3 decoy. The
authors should discuss this.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author
can be trusted to correct)

The manuscript contains various typos and mistakes in using the English language, although understanding
is not impedimented, editing by a native speaker is encouraged.

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major
compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published
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