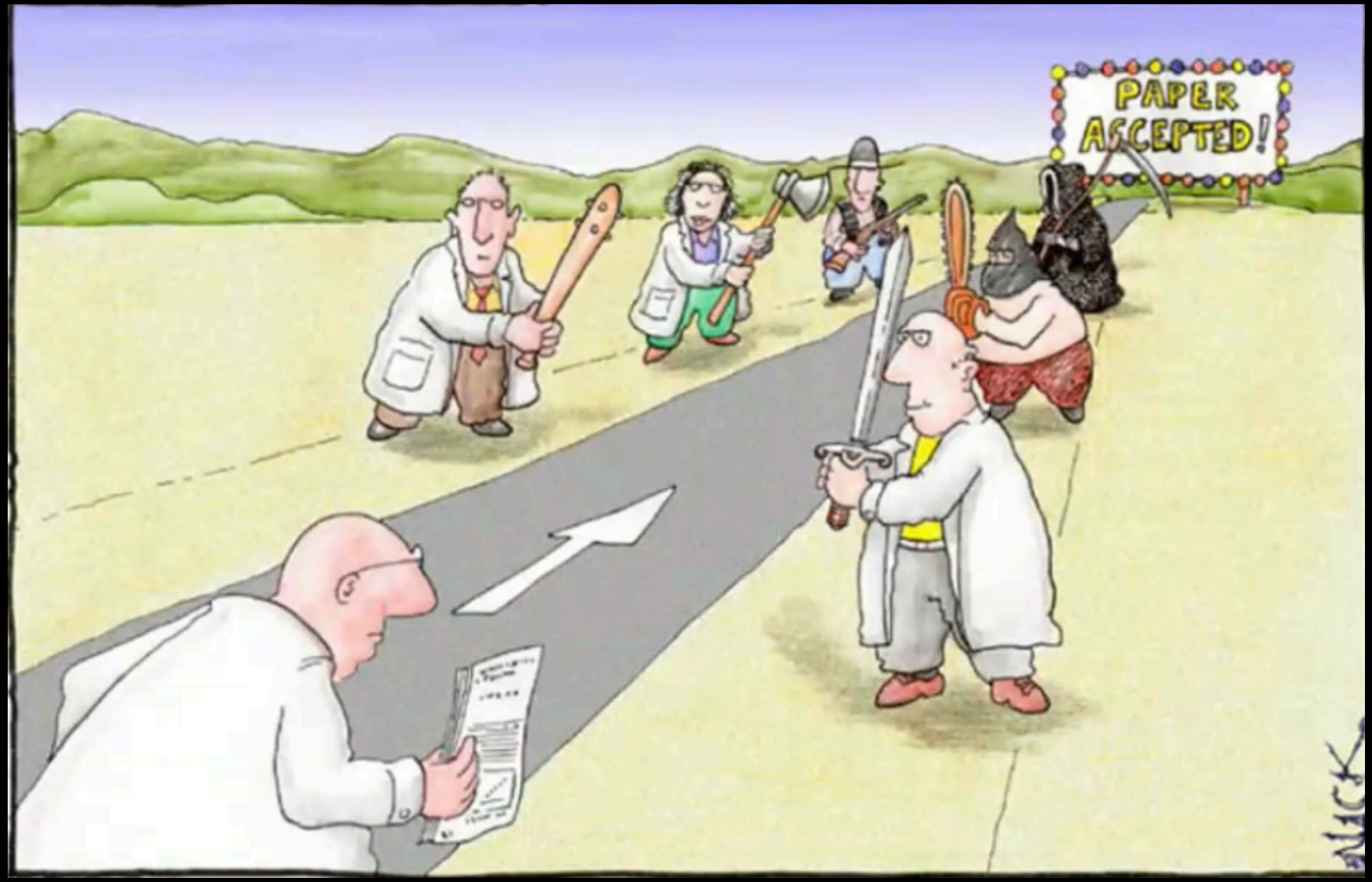
Writing a Scientific paper


PAPER ACCEPTED!

WHAT IS A STRONG MANUSCRIPT?

- Has a novel, clear, useful and exciting message
- Presented and constructed in a logic manner
- Reviewers and editors can grasp the significance easily

Suggestion by an editor:
editors and reviewers are busy scientists, make things easy and simple

QUESTIONS TO ANSWER BEFORE YOU WRITE
(*WHY YOU WANT TO PUBLISH YOUR WORK*)

Is it new and interesting?

Is it a current hot topic?

Have you provided solutions to some difficult problem?

Are you ready to publish at this point?

Before writing the paper

- Clearly identify the key message of the paper (be able to articulate it one clear sentence)
- The vision statement should guide all subsequent decisions
- Prepare draft version of figures and tables and prepare a storyboard

WHAT KIND OF PAPER

Full articles/ Original articles

Letters / Rapid communications / Case report

Review papers

New manuscript types (data in brief, Graphical reviews etc)

SELECT BEST JOURNAL FOR SUBMISSION

- Look at your references, this should help narrowing the choices
- Ask the following questions:

Is the journal peer reviewed at the right level?

Who is the journal's audience?

How fast does it make a decision or publish the paper?

What are the impact metrics of the journal?

Do you want/need open access?

Does the journal really exist? (check the Beall's list of predatory publishers)

COMMON PROBLEMS WITH MANUSCRIPT SUBMISSION

- Submission of papers clearly out of scope
- Failure to format the paper according to instructions
- Inappropriate suggested reviewers
- Inadequate English
- Resubmission of rejected paper without revision

AUTORSHIP: who is entitled to be an Author

Most commonly:

- Substantial contribute – from conception to interpretation
- Draft the article and revise it
- Give approval to the version
- Agree to be accountable
- All points required. Alternatively acknowledgements

AUTHORSHIP

FIRST AUTHOR Conduct or supervised the paper and submit (possible shared first authorship)

CORRESPONDING AUTHOR The first Author or a senior author

LAST AUTHOR the primary investigator of the project, provided daily supervision, frequently the group leader

<u>AVOID</u> GHOST AUTHORS
GIFT AUTHORS

How to choose supporting results

Once decided the key points of the paper see what to include

Keep what makes your paper better and discard everything else

Papers that contain lots of unrelated results are difficult to comprehend

Organise the paper as a movie. Scientists are story telling humans

Often the problem is not the writing: it is the thinking

WRITING PAPER – tips -

Reading is linear, writing does not have to

Scientific papers are stories not just containers of information

Well written paper are often about a single thing

Not every paper can be amazingly important, however every paper can be focussed, easy to understand and come with a clear take home message

If a result makes you go “that’s funny” it probably contains a story worth telling

Unexpected results can be turned into an exciting story

WRITING THE ABSTRACT(advertising)

“clear thinking becomes clear writing”

It takes some courage to write the abstract first, but it’s worth it

The abstract determines the story and it is critical for making the paper catchy. It is also the first thing that the reader sees!!

One common mistake is to view the abstract a linear string of equally important pieces of information to let the reader know what you have done. This is a boring abstract . The first few sentences are to provide context and excitement

Then the script continues with the problem to solve and the resolution.

Finally the epilogue that with few sentences should illustrate how your results have changed the world, first in your field and then more broadly

A common mistake is to end the abstract abruptly after the results. The reader is left alone to find the meaning of the results

THE ABSTRACT RESEMBLES A HOURGLASS

it answers two main *whats* :what has been done
what are the findings

- Starts by broadly introducing the setting
- Then narrows down to a specific research problem
- Then the solution found
- Then the hourglass widens again towards the
- Epilogue with the effects in the world

Graphical abstract may be placed next to the textual abstract to visually summarize the research in a single easy to follow figure

HOW TO CHOOSE THE TITLE

Maybe the most important part of the paper. The first thing the reader sees and condition his choice to keep on reading

- **Avoid unnecessary phrases such as " a study of"or "an investigation of"**
- **Avoid abbreviations**

The title has to be in perfect sync with the abstract – they have to tell the same story

- make sure that your title and abstract use the same words and concepts
- make sure that everything mentioned in the title is discussed in the abstract

Remove empty words " towards understanding problem x". *~~An investigation on~~ the influence of the color on the taste of apples*

In max 15 words tell: Purpose, Method and findings.
"Injured tendon regeneration induced by mechanically isolated amniotic stem cells"

Consider the possibility of having a "two sentences title"

Can Antibiotics make bacteria live longer? An investigation of….

Consider search engines

Cell Biology International

Cell Biol. Int. (2012) 36, 7–19 (Printed in Great Britain)

Research Article

Stemness characteristics and osteogenic potential of sheep amniotic epithelial cells

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Abstract

We set out to characterize stemness properties and osteogenic potential of sheep AEC (amniotic epithelial cells). AEC were isolated from 3-month-old fetuses and expanded *in vitro* for 12 passages. The morphology, surface markers, stemness markers and osteogenic differentiation were inspected after 1, 6 and 12 passages of expansion, with an average doubling time of 24 h. AEC clearly expressed the stemness markers Oct-3/4 (octamer-binding protein-3/4), Nanog, Sox2 and TERT (telomerase reverse transcriptase) and displayed low levels of global DNA methylation. Culture had moderate effects on cell conditions; some adhesion molecules progressively disappeared from the cell surface, and the expression of Sox2 and TERT was slightly reduced while Nanog increased. No changes occurred in the levels of DNA methylation. Cells organized in 3D spheroids were used for IVD (*in vitro* differentiation). Within these structures the cells developed a complex intercellular organization that involved extensive intercellular coupling despite continuous cell migration. Marked deposition of calcein in the ECM (extracellular matrix), increased ALP (alkaline phosphatase) activity, expression of bone-related genes (osteocalcin) and the matrix mineralization shown by Alizarin Red staining demonstrate that AEC can undergo rapid and extensive osteogenic differentiation. AEC introduced in experimental bone lesions survived in the site of implantation for 45 days and supported consistent bone neoformation, thus showing promising potential applications in osteogenic regenerative medicine.

Keywords: amniotic epithelial cells (AEC); amniotic stem cells; bone repair; differentiation; osteogenesis; sheep

Selecting a Single Embryo for Transfer after *In-vitro* Fertilization: A Translational Medicine Perspective

Abstract

Apart from the huge efforts made to develop an embryo in-vitro, the embryologist is faced with an even bigger task to choose an embryo from a cohort that will produce pregnancy. Selecting a single viable one is often a challenge to the embryologists and clinicians involved. This is because the one that is selected may determine outcome of the cycle. It is not in the embryologist interest to choose an unhealthy embryo that will allow patients suffer emotionally or financially. A responsible professional often seeks way to select embryo that will make a baby. There are several methods that have been introduced for this purpose since the birth of Louis Brown in 1978. These methods include the traditional embryo morphology grading system, newer technologies like time lapse monitoring, pre-implantation genetic screening, metabolomics, proteomics and transcriptomics. There are conflicting claims that these newer technologies are superior to the morphology grading system. This paper however, advocates for a holistic system that is capable of analyzing all the pathways in an embryo to provide a general health picture. Newer technologies for embryo selection and the traditional embryo grading system in its present form have not achieved 100% accuracy in selecting a single embryo. Research into a holistic system capable of selecting a single embryo will be ideal and better driven by a translational research team that will provide an interdisciplinary and multi-frontier approach. We have described here an elementary version of such a system with the hope that it simplicity, rapid turnaround time and cost effectiveness will encourage it application in IVF. This diagnostic platform may be developed for use in IVF laboratory in the future to select the most appropriate embryo.

Keywords: *In-vitro* fertilization; Oocyte; Sperm; Embryo; Endometrium and Methods of evaluation

Sympathetic Reinnervation is Required for Mammalian Cardiac Regeneration

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Abstract

Rationale—Although mammalian cardiac regeneration can occur in the neonatal period, the factors involved in this process remain to be established. As tissue and limb regeneration require concurrent reinnervation by the peripheral nervous system, we hypothesized that cardiac regeneration also requires reinnervation.

Objective—To test the hypothesis that reinnervation is required for innate neonatal cardiac regeneration.

Methods and Results—We crossed a Wnt1-Cre transgenic mouse with a double-tandem (td) Tomato reporter strain to identify neural crest-derived cell lineages including the peripheral autonomic nerves in the heart. This approach facilitated the precise visualization of subepicardial autonomic nerves in the ventricles using wholemount epifluorescence microscopy. Following resection of the left ventricular apex in 2-day-old neonatal mice, sympathetic nerve structures, which envelop the heart under normal conditions, exhibited robust re-growth into the regenerating myocardium. Chemical sympathectomy inhibited sympathetic regrowth and subsequent cardiac regeneration following apical resection, significantly (scar size as cross-sectional percentage of viable LV myocardium: n=9, 0.87±1.4% vs. n=6, 14.05±4.4%; $p<0.01$).

Conclusions—These findings demonstrate that the profound regenerative capacity of the neonatal mammalian heart requires sympathetic innervation. As such, these data offer significant insights into an underlying basis for inadequate adult regeneration following myocardial infarction, a situation where nerve growth is hindered by age-related influences and scar tissue.

Evaluation of in vitro fertilization outcomes using interleukin-8 in culture medium of human preimplantation embryos

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[a] Reproductive Medicine Center, Department of Obstetrics and Gynecology, Affiliated Hospital of Guizhou Medical University, Guiyang; [b] Multidisciplinary Research Center, Shantou University, Shantou; and [c] Department of Urinary Surgery, Affiliated Hospital of Guizhou Medical University, Guiyang; and [d] Department of Gastroenterology, Second Affiliated Hospital, Shantou University Medical College, Shantou, People's Republic of China

Objective: To investigate whether selected cytokines are detectable in the embryo culture medium (EM) of human preimplantation embryos (HPE) and what the relationship is of the cytokines with clinical outcomes.
Design: Cross-sectional study.
Setting: University-affiliated tertiary teaching hospital.
Patient(s): Three-hundred and thirty infertile women who underwent fresh cycle in vitro fertilization (IVF) between January and December 2014.
Intervention(s): Collection on the day of transfer of the EM of each embryo that was transferred in all patients for measurement of cytokine levels.
Main Outcome Measure(s): Measurement of 13 selected cytokines in the EM of day-3 HPE to analyze the relationship of the cytokine with embryo quality and clinical outcome.
Result(s): Of the cytokines measured, only interleukin-8 (IL-8) was statistically significantly associated with clinical outcome. The rate of detectable IL-8 in the EM was 32.42%, and the pregnancy rate, implantation rate, and number of live births per in vitro fertilization (IVF) or intracytoplasmic sperm injection patient (N LBPP) were higher, and O IR was lower in patients for whom the medium from transferred embryos was positive for IL-8 (IL-8 positive group) compared with the patients for whom the medium tested negative for IL-8 (IL-8 negative group). Compared with the IL-8 negative group, a higher pregnancy rate was observed in the IL-8 positive group when the patients received equal good–ordinary quality embryos.
Conclusion(s): In the EM from HPE, IL-8 is associated with higher pregnancy rates, higher IRs, and higher N LBPP, so IL-8 may be an independent predictor for pretransfer assessment of the embryo development potential in IVF patients. (Fertil Steril® 2017;107:649–56. ©2016 by American Society for Reproductive Medicine.)
Key Words: Culture medium, embryo quality, interleukin-8, IVF outcome

Discuss: You can discuss this article with its authors and with other ASRM members at https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/13575-22911

Anatomy of a scientific paper

INTRODUCTION
What is known

What is unknown , what is the gap to fill

How and why should we fill the gap

METHODS

RESULTS
What did you get

DISCUSSION
How the results fill the gap

CONCLUSION
What does this mean for us

INTRODUCTION

“the reasons why you did the study”

- Establish the context of the research
- Define gaps in knowledge that the study will fill
- State the aims of the paper with questions and hypotheses
- Give rationale of the work
- Anticipate main results (according to guidelines of the journal)

Four paragraph template to write the introduction

First paragraph. THE CONTEXT

Since it leads into the story the first couple of sentences are crucial. In addition to the context it set the excitations

- Say the knowledge gap with a powerful sentence
- After a strong beginning continue with a overview of the state of art
- You don’t need to tell the details. Cite proper review instead
- End the paragraph with some contrast “despite all this, we do not fully understand …..” or “however the role of X remains an open question

Example

Here is the beginning of the first paragraph of Altarelli et al., Phys. Rev. Lett. 112, 118701 (2014): “Tracing epidemic outbreaks in order to pin down their origin is a paramount problem in epidemiology. Compared to the pioneering work of John Snow on 1854 London’s cholera hit [1], modern computational epidemiology can rely on accurate clinical data and on powerful computers to run large-scale simulations of stochastic compartment models. However, like most inverse epidemic problems, identifying the origin (or seed) of an epidemic outbreak remains a challenging problem…”

Second paragraph
(zoom in your particular problem)

- If the first paragraph ends by saying " the reason for the tendon failure to repair is not fully understood yet" you can begin the second paragraph by explaining why that question is important and why hasn't it been solved
- Continue by explaining why answering that question is worthwhile and if others have tempted to solve the problem
- Use carefully chosen citations to emphasize what is known
- At the end of this paragraph clearly state the research question that your paper addresses

Third paragraph

The point of view moves from what others have done, to how you have approached this question
Example: “to this aim we have carried out an experiment where…..”

Describe what the study will do

Use clear phrase to introduce aims
“the purpose of this study was….”
“The objective of the study is…..”
“We investigated a possible mechanism----”

Key verbs: describe, investigate, present, analyse, assess

The Statement of Purpose is usually placed at
the end of the introduction

The rationale of the approach

Address these questions

- Why this kind of approach
- What are the advantage of the model
- Why this technique is better than previous ones

Fourth paragraph

The paragraph moves from your approach to your findings . It reveals the outcome of your work and briefly summarise your results. Eventually anticipate impact on the world

Usually keep this paragraph clear and short

Tips for the introduction

Use highly relevant sources to support the study

Use keywords from the title to focus the exact problem

Include an hypothesis

Use only articles highly related to the study and review articles for summarizing context

Keywords

Cardiac regeneration; neonatal repair; cardiac innervation; sympathetic denervation; neonatal mouse cardiac myocyte; sympathic nervous system

INTRODUCTION

It has recently been established that unlike the limited cardiac regeneration demonstrated by the injured adult mammalian heart, the neonatal heart remains permissive for near-complete cardiac regeneration during a finite developmental period[1, 2]. In a similar fashion to other regeneration-competent species including the salamander[3] and zebrafish[4, 5], the dominant mechanism underlying cardiac regeneration in the neonatal mouse appears to be de-differentiation and proliferation of resident cardiac myocytes[2]. However, the underlying basis for regeneration and revascularization of the neonatal tissue are not fully understood. Other vertebrate[6–9] and invertebrate[10] models of tissue regeneration exhibit a complete dependence on reinnervation of the regenerating tissue by nerves of the peripheral nervous system (PNS). Despite the clinical importance of cardiac autonomic innervation, the neuroanatomy of the sympathetic nerve plexus innervating the ventricular myocardium remains incompletely characterized[11].

To address these issues, we used a combination of genetic and pharmacologic tools to map the cardiac PNS and to test the role of peripheral nerve innervation in mammalian cardiac regeneration. Post-ganglionic, subepicardial sympathetic axons make up the bulk of nerve fibers in the ventricles[11] and we demonstrate, for the first time, that these nerve fibers undergo robust re-growth and reinnervation during the regeneration of resected ventricular tissue. Furthermore, sympathectomy abrogates cardiac regeneration and promotes collagenous scar formation, demonstrating that innate mammalian cardiac regeneration in neonates is dependent on sympathetic innervation. Together these findings suggest that concurrent reinnervation of injured adult cardiac tissue is essential for functional and complete cardiac regeneration.

INTRODUCTION

Inhibin, a hetero-dimeric glycoprotein comprised of two subunits in the form of inhibin A ($\alpha\beta_A$) and inhibin B ($\alpha\beta_B$) (de Kretser et al., 2000), plays an essential role in regulating pituitary follicle-stimulating hormone (FSH) synthesis and secretion. Immunization against inhibin has been used to increase animal reproduction and fertility. The development of an inhibin immunogen has involved conventional protein and novel DNA phases. Many studies have demonstrated that immunization against native inhibin preparations purified from follicular fluid (Morris et al., 1991; Sewani-Rusike and Dakwa, 2000), those that are chemically synthesized (Tannetta et al., 1998), or genetic fragments of the inhibin α-subunit (O'Shea et al., 1993; Li et al., 2009, 2011; Wang et al., 2009) stimulated follicular development and enhanced oocyte quality, maturation competence (Li et al., 2009), and sperm quality (Avital-Cohen et al., 2012). The preparation and purification of a conventional vaccine is time-consuming and labor-intensive. Because of their convenience, stability, and cost, a variety of DNA vaccines encoding the inhibin α (1-32) gene or a fusion with the S gene of the hepatitis B surface antigen have been developed (Han et al., 2008; Wang et al., 2012), and the results showed that an inhibin DNA vaccine was a promising tool for improving animal fertility. However, DNA vaccines face several problems such as low-uptake efficiency (Greenland et al., 2007), dose-dependence (Huang et al., 2008), low immunogenicity in humans and large animals (Melkebeek et al., 2007), and, particularly, antibiotic-resistance-based plasmid selection systems (Galen et al., 2010), making it important to develop an alternative approach for inhibin DNA vaccination.

Attenuated *Salmonella choleraesuis* can transfer plasmids encoding foreign antigens under the control of a eukaryotic promoter to host cells, protecting against the bacteria itself, allowing simultaneous immune responses specific to the heterologous antigen(s) (Kwon et al., 2007), and strong humoral and cellular responses (Yang et al., 2010). Therefore, this system is considered to be an ideal candidate for the delivery of DNA vaccines. In addition, incorporation of a balanced lethal vector system can minimize the risks of antibiotic use (Torres-Escobar et al., 2010).

In our present study, we applied a balanced lethal bacteria vector system for the inhibin vaccine. This system involved the use of an artificial mutant of an *S. choleraesuis* C500 strain capable of double deletion of the cyclic AMP receptor protein (*crp*) and β-aspartic semialdehyde dehydrogenase (*asd*) genes, and an inhibin recombinant plasmid, pVAX-IS-*asd* (pXAIS), without antibiotic resistance based on a previous study (Han et al., 2008; Zhen et al., 2009). The objectives of this study were to determine the safe dosage of the *S. choleraesuis*-mediated vaccine and to assess the effect of this vaccine on the serum antibody titer against inhibin and follicular development in rats.

METHODS

STEP 1

- Prepare figures and tables
- Gather all data
- Give them number and captions
- Place them in the order to show in the results

STEP 2
- how the study was carried out and analysed

How the experiments were done (when the experimental design is complex you may use a diagram)

Why the procedures were chosen

How results were analysed

Statistical methods used

Materials and methods

This section serves two purposes:

1. Let other researcher gauge whether your conclusions are justified and backed up by evidence
2. Allow other researchers to replicate your study

- Top journal style (PNAS, Nature etc.) is to have Materials and Methods as a separate section at the end of the article as an appendix.

- In biomedical journal style Methods are described in all their detail straight after the introduction. The downside is that reading the paper may be deadly boring

Explain what you have done in as much detail as possible.
Release your raw data, your intermediate results.
Hide nothing. Be a good scientist.

STEP 2 methods

1. Material used and origin
2. Material preparation
3. Measurement methods

- Preparations and measurements organized chronologically
- List methods in the order used for results
- Order from most to less important

Do not repeat details of published methods: use references and supporting materials

- Methods maybe about 10% of the paper. (see journal guide)
- Use past voice and past tense
- Do not discuss the results

Heat inactivated serum was purchased from Sigma (sede)
Amniotic membrane was….
A laser confocal microscope was used to assess..

Figures

- tables give the actual experimental results, while figure are often used for comparisons of experimental results
- Whatever your choice is, no illustrations should duplicate the information described elsewhere in the manuscript
- figures and table legends must be self-explanatory
- Lines joining data only can be used when presenting time series or consecutive samples data. When there is no connection between samples or there is not a gradient, you must use histograms

RESULTS part 1. Figures

Outline the results with figures and their order

Define order within each category. The order should tell a clear story with each figure built on the previous one

Write captions for figures and tables before the results

Make sure that your captions reflect what the reader should learn. A caption that says : “here we see Y plotted as a function of X” is useless. This should be clear by the axis labels. Always tell the reader what he should see in the figure, how to interpret it.

Use colour consistently throughout your figures and pay attention to the font size

Figures must be professional

RESULTS part 2. text

Recall the research question of the introduction

Present findings in the same order as the Methods (use subsections)

Present data responding to the question without discussing

Add secondary results

Present data in Figures, tables and text

Never start a sentence “As shown in fig…” but refer the reader to figure
at the end of the sentence … as shown in fig.

Don’t say preliminary introducing sentence such as
“ plant growth was conditioned by soli salinity”
but say “plant A grew faster than plan B in high salinity”

WRITING THE DISCUSSION
(in some journals discussion is integrated in the results)

Scientists are often scared to make confident statement with muscularity. The result is a turgid obfuscatory writing that sounds defensive. Be convincing.

- Begin the discussion by reminding the reader the broader knowledge gap and the specific question of the paper
- Give some examples and state of art of more recent investigations
- Explain why the gap has not been filled yet and then proceed through your results one by one or grouping them to certain points
- Contextualise the results within the literature, how do the results agree with previous work in the literature.
- Cite yourself without overdoing
- Show how the results contribute to solve the broader problem pointed out in the abstract and the introduction

Writing the discussion: tips

- Avoid statements that go beyond what the results can support
- Avoid unspecific expression (high temperature, low rate… be specific)
- Avoid sudden introduction of new terms and new ideas

At the end It is common to discuss the limitation of your work but this should not be the first time they are mentioned. Let the reader know about them earlier, be open from the very beginning

> *Instead of saying that your results would be even clearer if your experimental set up had a higher resolution, say that even though the resolution of your experimental set up is limited your results are nevertheless quite convincing (say "but, yes" instead of "yes, but")*

Instead stating that further research is required go for:
Because of the results of this paper it is now possible to tackle
problem X with method Y to come closer to the ultimate goal of Z

Ending the paper you can use the words
"with this study we have shown that…

DISCUSSION what is the meanings of the results

"Countless manuscript are rejected because the discussion section is so weak. Results should be put into a global context to demonstrate what makes those results significant or original"

Questions to answer:

1. Are results related to research aims

2. Do the results agree with each other

3. Data support the hypothesis proposed

4. Compare with other studies

1. What are the study implications

2. Further research required

CONCLUSIONS

- Underline how results fit with the aims of the research
- Briefly show how your results improve knowledge
- Put your work into perspective, indicate extension and further implications

the cover letter

- Begin by stating the paper's title and the type of paper you are submittnig (review, short communication, research)
- Concisely explain why your study was performed, what was done and what are the key findings
- State why the results are important and what impact they may have in the field
- Make sure you mention how your approach and findings relate to the scope of the journal to show why the article would be of interest to its readers
- In the last paragraph state that the work is original and that you have not submitted it for publishing elsewhere