From: Stephen Quake [quake@stanford.edu]
Sent: Monday, July 07, 2008 12:04 PM
To: Yair Blumenfeld; Christina H. Fan
Cc: Stephen Quake
Subject: Re: latest version

Christina

I am about to send you more edits. This would also be a good time to talk on the phone. You can call my french cell at +33 642 702902

Steve

Stephen Quake
Professor of Bioengineering
Stanford University

NOTE NEW EMAIL: quake@stanford.edu

-----Original Message-----
From: Yair Blumenfeld <yairb@stanford.edu>

Date: Mon, 07 Jul 2008 10:50:23
To: Christina H. Fan<chfan@stanford.edu>
Cc: Stephen Quake<quake@stanford.edu>
Subject: Re: latest version

Hi Christina,

It looks great. I think I answered most of the comments you directed towards me and I added a little bit about the recent ACOG Practice Bulletin which recommends that invasive testing now be offered to ALL women, regardless of risk factors. I think it will play nicely with the need for a "risk-free" non-invasive diagnostic test.

Thanks,

Yair

Quoting "Christina H. Fan" <chfan@stanford.edu>:

> hi steve, yair
> this is the latest version of i have
> the changes i made are:
>
> 1.
> i added the references, but i couldn't find the JGI paper (not exactly
> sure which one it is) and any relevant references for dr. snyder
>
> 2.
> i added 2 or so paragraphs in the discussion
> one of the main one is the 'problem' with our samples that they are
> collected after amnio or CVS, according to yair. i am sure dr. bianchi
> would raise that question if we choose not to mention it in the
> methods because in a paper she and dennis lo wrote they made it a big
> deal..
>
> 3.
> i think besides microchimerism, we should mention confined placental

> mosacisim since it seems more relevant for the case of cell-free dna
> since these dna potentially come from the placenta...but i have gone
> deep enough to be able to find references regarding how much of the
> placenta usually has mosacisim..yair, do you think you have any
> references you can think of to address this issue?
>
> 4.
> the graphs
> for figure 1a, i changed the order of the chromosomes according to
> there GC content as steve suggested and it looks visually much better
>
> for figure 2, i added the fetal DNA fraction estimated from chrX and
> chrY... thus figure 1c is probably not neccesary..and figure 1d
> probably isn't necessary as well (can put in supporting info)
>
> for figure 3b, i added the graph of cumulative fetal fraction
>
> 5.
> i still dont' know what to do with the outlier point (P13)
> it probably doesn't affect figure 1a and 1b (it is currently included
> in figure 1a and 1b)
> but when it comes to estimation of fetal DNA fraction...the estimation
> is based on the comparison to female pregnancies (chrX) or male donor
> plasma (chrY)..and in figure 1c...you can see that P13 has chrX
> coverage even higher than female pregnancies..which doesn't seem to
> make sense... currently P13 is not included in the estimation of fetal
> dna fraction using chrX and chrY data...
> what should we do??
>
> 6.
> one last thing that i still haven't solved..
> i think we need a better way of estimating the limit of our test..the
> use of a 95% confidence interval based on the coverage data of normal
> pregnancies doesn't make too much sense to me after i thought about
> it...the sensitivity should somehow incorporate sampling rate (how
> much we are sampling) which is not reflected by the 95% CI..
> however, due to sequencing bias, the sampling no longer follows
> poisson distribution..the distribution of the number of tags per 50kb
> window deviates from normal and are skewed to the right...i have been
> thinking about this problem for a while and i haven't come up with a
> solution..perhaps steve would have a better idea??
>
> 7.
> added the remaining graphs of TSS from other samples in the supporting
> information
>
> i will be back in the lab at 10.30am tmr
>
> christina
>
>
> Quoting Stephen Quake <quake@stanford.edu>:
>
>> ok i have done a bunch of editing and have a lot of questions (sorry
>> to give you such a busy weekend, but it will be worth it - this is
>> shaping up into a great paper!)
>>
>> please accept the changes i made and then track any further changes
>> you make. let me know if you want to speak on the phone tomorrow. my
>> usa cell works and is 626 274 5841 and it is +9 hours from you.
>>
>> one thing we must do is work in references to mike snyder, eddy rubin
>> and diana bianchi since we know they are referee candidates. i have
>> indicated where to do this for the last two but not for mike yet. he
>> recently publishd something on down syndrome so it shouldn't be too
>> tough.

>>
>> best
>>
>> steve
>>
>> --
>> ----------------------
>> Stephen Quake
>> Professor of Bioengineering
>> Stanford University
>>
>> PLEASE REPLY TO: quake@stanford.edu
>>

Yair Blumenfeld
Maternal-Fetal Medicine Fellow
Department of Obstetrics & Gynecology
Stanford University