From: srquake@gmail.com on behalf of Stephen Quake
To: Leonard A. Herzenberg
Cc: Christina Fan; Yair Blumenfeld
Subject: Re: favor re: pnas
Date: Wednesday, July 09, 2008 3:20:54 AM
Attachments: noninvasive_v1.5.pdf

---

sorry, here is the attachment...

On 7/8/08, Leonard A. Herzenberg <LenHerz@darwin.stanford.edu> wrote:
> Steve,
> There was no attached mss.
> Len
>
> -----Original Message-----
> From: srquake@gmail.com [mailto:srquake@gmail.com] On Behalf Of Stephen Quake
> Sent: Tuesday, July 08, 2008 2:47 PM
> To: Leonard A. Herzenberg
> Cc: Christina H. Fan; Yair Blumenfeld
> Subject: Re: favor re: pnas
>
> Len,
>
> Here is the manuscript - hope you enjoy it!
>
> best,
>
> Steve
>
> On 7/1/08, Stephen Quake <quake@stanford.edu> wrote:
> > Many thanks for doing this. I will get you the mss early next week.
> >
> > Steve
> > ---------------
> > Stephen Quake
> > Professor of Bioengineering
> > Stanford University
> >
> > NOTE NEW EMAIL: quake@stanford.edu
> >
> >
> > -----Original Message-----
> > From: "Leonard A. Herzenberg" <LenHerz@darwin.stanford.edu>
> >
> > Date: Tue, 1 Jul 2008 22:37:01
> > To: quake@stanford.edu<quake@stanford.edu>
> > Subject: RE: favor re: pnas
> >
> >
> > Steve,
> > I thought you would so I'm not disappointed. So send me the mss in form for PNAS and I'll send it to two of the three referees recommended by you plus Diana. That way I will maintain "secrecy".
> > When can I expect your mss which I'll read first. If I accept it,
> > I'll have the PNAS office send to the two referees.
> > Len
> >
> >
> > -----Original Message-----

> > From: Stephen Quake [mailto:quake@stanford.edu]
> > Sent: Tuesday, July 01, 2008 10:27 PM
> > To: Leonard A. Herzenberg
> > Subject: Re: favor re: pnas
> >
> > Yes I know about microchimerism and we are not sensitive to it since we are effectively sampling dna from many cells, only a tiny fraction of which might be chimeric. I will put in a paragraph discussing this.
> >
> > Diana wouild be a great referee, I know about her work but didn't realize she trained with you.
> >
> > Best
> >
> > Steve
> > ---------------
> > Stephen Quake
> > Professor of Bioengineering
> > Stanford University
> >
> > NOTE NEW EMAIL: quake@stanford.edu
> >
> >
> > -----Original Message-----
> > From: "Leonard A. Herzenberg" <LenHerz@darwin.stanford.edu>
> >
> > Date: Tue, 1 Jul 2008 13:35:00
> > To: Stephen Quake<quake@stanford.edu>
> > Subject: RE: favor re: pnas
> >
> >
> > Hi Steve,
> > Do you know of microchimerism? The women (mothers here) who had received fetal cells from a former pregnancy or from their mothers or by exchange of blood with twins (non-identical) from a prior pregnancy maintain these cells, probably in their bone marrow. Then in tissues having an autoimmune manifestation will contain these microchimeric cells. That might lead to plasma having DNA from other sources than the current pregnancy.
> > This was written up in a Scientific American Article by J. Lee Nelson earlier this year in Feb. I think.
> > Has you mss taken this into account?
> > If so, I'd like one of your reviewers be Diana Bianchi, a former med student of mine from the '70s, who discovered with me and my lab fetal cells in maternal blood. She is now a Prof at Tufts Univ Med School in Boston.
> > If all goes well, I could communicate your mss to PNAS.
> > Len
> >
> > -----Original Message-----
> > From: srquake@gmail.com [mailto:srquake@gmail.com] On Behalf Of Stephen Quake
> > Sent: Tuesday, July 01, 2008 11:44 AM
> > To: Leonard A. Herzenberg
> > Subject: favor re: pnas
> >
> > Len,
> >
> > I have a favor to ask. We are doing a clinical study on cell-free DNA
> > found in the blood of pregnant women. As you may know, a significant
> > (~3%) portion of this of fetal origin. We used next-generation
> > sequencing to sequence huge amounts of this dna, and found, among
> > other things, that we can map the fragments back to their chromosomes
> > of origin and use the statistics of this mapping to diagnose whether
> > or not the fetus has an aneuploidy such as down syndrome. this is a
> > big deal as it enables a non-invasive test for down syndrome, so amnio

> > and cvs (and the risk to the fetus that they pose) can be retired. we
> > have been in a hot race with groups in hong kong and basel to achieve
> > this, and i am worried that we might get scooped.
> >
> > would you be willing to communicate the manuscript to pnas for us, and
> > fairly rapidly? if so, and if it would be useful to you, i have also
> > found two distinguished scientists who work at the interface of
> > genomics and human health who are willing to referee with a fast
> > turnaround (i don't collaborate with either): mike snyder (yale) and
> > eddy rubin (director of the doe joint genome institute).
> >
> > hope you are well,
> >
> > steve
> > --
> > ----------
> > Stephen Quake
> > Professor of Bioengineering
> > Stanford University
> >
> > PLEASE REPLY TO: quake@stanford.edu
> >
>
>
> --
> ----------
> Stephen Quake
> Professor of Bioengineering
> Stanford University
>
> PLEASE REPLY TO: quake@stanford.edu
>

--

Stephen Quake
Professor of Bioengineering
Stanford University

PLEASE REPLY TO: quake@stanford.edu

Classification:
Major – Biological Sciences
Minor – Medical Sciences

Title:
Noninvasive Diagnosis of Fetal Aneuploidy by Shotgun Sequencing DNA from Maternal Blood

Author affiliation:
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Manuscript Information:
Number of text pages:
Number of figure:
Number of tables:

Abbreviations:
T21: trisomy 21

Abstract

We directly sequenced cell-free DNA from plasma of pregnant women with high throughput shotgun sequencing technology, obtaining on average a few million sequence tags per patient sample. This enabled us to measure the over- and under-representation of chromosomes from an aneuploid fetus. The sequencing approach is polymorphism-independent and therefore universally applicable for the non-invasive detection of fetal aneuploidy. Using this method we successfully identified all 7 cases of trisomy 21 (Down syndrome) in a cohort of 13 normal and aneuploid pregnancies; trisomy 21 was detected at gestational ages as early as the 14^{th} week. Direct sequencing also allowed us to study the characteristics of cell-free plasma DNA, and we found evidence that this DNA is enriched for sequences from nucleosomes.

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