

From: [John West](#)
To: [Christian Haudenschild](#)
Cc: chaudenschild@personalis.com; [Mark Pratt](#); [Carol Tillis](#); [Richard Chen](#)
Subject: Confidential : Personalis laboratory plans
Date: Monday, April 2, 2012 9:12:57 AM

Hi Christian,

Part of Personalis' plan is to be able to accept samples from customers, sequence them, and provide the medical analysis of the genomes. The lab analysis may include multiple assays from the same sample, both NGS and other (e.g. Electrophoretic fragment analysis, arrays, FISH, etc). Our goal is to be accurate, comprehensive and validated. To that end, our NGS may include both whole genome and deeper sequencing of some regions selected by pull out. Mark Pratt is working on lists of regions we may want to pull out. Some of the pullout may be to sequence with a second paired-end insert length (likely quite long).

We are also thinking about how to incorporate RNAseq (Mark Pratt can get you a copy of the recent "Snyderome" paper, for some of our thinking on that.

We expect to outsource the whole genome NGS, but might want to do the targeted sequencing ourselves. We have budgeted a MiSeq for that, both to be able to look at smaller amounts of sequence and for the longer reads.

As far as arrays go, we are interested in fluorescence intensities, not just genotypes, for validation of structural variants. We have been thinking about use of the Illumina 5M and exome arrays. We are also thinking about a custom array based on the content in our highly curated databases. Arrays are inexpensive relative to whole genome sequencing, so even if we need more than one array type per sample, it could be OK.

For all this, we will need an ability to receive samples and divide them up both for the initial assays but also for follow on validation. This means we will need a system to handle, QC, track and store samples. Initially we expect these may be DNA or cell lines (e.g. Coriell) but later these to include blood and saliva samples. Initially we may outsource a lot and then selectively pull more in house, especially our proprietary assays.

We will need to practice on samples and have been thinking about a few projects for this:

1. Craig Venter's DNA, available through Coriell, as the only single-person whole genome Sanger sequence, for genome-wide comparison of NGS vs Sanger.
2. A large family or two, with at least 4 children / family and all four grandparents. This is to use Mendelian Inheritance as a check for the results obtained from the individual genomes. We have data from one family quartet now, but the data is from late 2009. We would like modern data from individuals who have no relationship with the company.
3. Samples with triplet repeat expansions already validated by electrophoresis fragment analysis (e.g. Huntington's samples from Coriell). We have ideas for how to sequence these with NGS.

Can you please work with Carol, Mark & Rich, cc'ed here, to develop a plan for this, including facilities, staffing, CapEx, IT, potential outsource partner labs, what needs to be CLIA and how we can be CLIA if we outsource, HIPPA, etc. There will be many specifics to be worked out and I look forward to discussing this with you more.

Thanks and again, Welcome on board.

John West

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On Apr 1, 2012, at 1:36 PM, Christian Haudenschild <chaudenschild@sonic.net> wrote:

> Excellent have a nice trip and enjoy the snow.

> Christian

>

>

> Sent from my iPhone

>

> On Apr 1, 2012, at 7:48, John West <john.west@personalis.com> wrote:

>

>> Hi Christian,

>>

>> Welcome on Board !

>>

>> My son's high school has spring break

>> this week so we will be away at

>> Whistler skiing. I will be on email

>> by iPhone early each morning and

>> each evening and will be back in the

>> office Monday next week (April 9th).

>> I apologize for being away your first

>> week, but look forward to catching up

>> next week.

>>

>> I will send you a number of emails

>> with background reading, etc.

>>

>> Carol Tillis has been making arrangements for your office, computer, etc, and will have your on-boarding papers. FYI we will be moving fairly soon, so we expect

>> to have better offices shortly.

>>

>> I have asked Mark Pratt to look out

>> for you and to introduce you to some

>> of what we are doing.

>>

>> As you may know, Scott Kirk (also ex-

>> Illumina Hayward) will also be starting

>> tomorrow, working for Rich Chen in a

>> role related to R&D project management.

>>

>> You also have a Personalis email

>> account, which I am cc'ing here.

>> You should already be able to

>> access it, but in case not, Carol should

>> be able to help.

>>

>> Again, I apologize for not being there

>> this week, but I look forward to seeing

>> you on the 9th.

>>

>> John West

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