

From: [Young, Daniel W.](#)
To: ["Greg Porreca"](#)
Cc: [Waller, Patrick](#)
Subject: RE: G0871.70000US00; METHOD FOR REDUCING REPRESENTATIONAL BIAS IN MULTIPLEX AMPLIFICATION OF NUCLEIC ACIDS (Porreca)
Date: Friday, April 24, 2009 7:03:51 PM
Attachments: [G0814.70002US00 CLAIMS.doc](#)

Hi Greg,

Please see the attached claims for Uri's application. Please let us know your comments.

Thanks
Dan

-----Original Message-----

From: Young, Daniel W.
Sent: Friday, April 24, 2009 4:38 PM
To: 'Greg Porreca'
Cc: Waller, Patrick
Subject: G0871.70000US00; METHOD FOR REDUCING REPRESENTATIONAL BIAS IN MULTIPLEX AMPLIFICATION OF NUCLEIC ACIDS (Porreca)

Greg,

Attached is an updated version of the above-mentioned application for you to review. I will forward you a revised set of claims for Uri's application later today. In the meantime, could you send me a document containing the final figures for Uri's application.

Thanks
Dan

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ML-IPR-000415

Claims

1. A method of analyzing a plurality of genetic loci, the method comprising:
 - (i.) amplifying a plurality of nucleic acids, each nucleic acid in the plurality having a polymorphic sequence and a barcode sequence;
 - (ii.) determining the frequency of occurrence of barcode sequences in the amplified plurality of nucleic acids, and
 - (iii.) if the frequency of occurrence of a specific barcode sequence in the amplified plurality is different from its frequency of occurrence before amplification, detecting bias in the amplification of the nucleic acid having the specific barcode sequence.
2. The method of claim 1, further comprising genotyping a polymorphic sequence of a nucleic acid in the plurality, wherein the genotyping comprises correcting for bias, if detected.
3. The method of claim 3, wherein the polymorphic sequence is selected from Table 2.
4. A method of analyzing a plurality of genetic loci, the method comprising:
 - (i.) amplifying a plurality of nucleic acids, each nucleic acid in the plurality having a barcode sequence, wherein the frequency of occurrence of each barcode sequence in the plurality is about equal to the frequency of occurrence of each other barcode sequence in the plurality;
 - (ii.) determining the frequency of occurrence of barcode sequences in the amplified plurality of nucleic acids, and
 - (iii.) if the frequency of occurrence of a specific barcode sequence in the amplified plurality is different from its frequency of occurrence before amplification, detecting bias in the amplification of the nucleic acid having the specific barcode sequence.

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5. The method of claim 4, wherein each nucleic acid in the plurality further comprises a polymorphic sequence.

6. The method of claim 5, further comprising genotyping a polymorphic sequence of a nucleic acid in the plurality, wherein the genotyping comprises correcting for bias, if detected.

7. The method of claim 6, wherein the polymorphic sequence is selected from Table 2.

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