[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, HHS

ACTION: Notice

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

SUPPLEMENTARY INFORMATION:

Mutations in the G Protein Coupled Receptor (GPCR) Gene Family in Melanoma

Description of Technology: Using exon capture and next generation sequencing approaches to analyze the entire G protein coupled receptor (GPCR) gene family in melanoma, the researchers at the NIH have identified several novel somatic (e.g., tumor-specific) alterations. GPCRs play an integral part in regulating physiological functions and the importance of these molecules is evident by the fact that approximately half of the current FDA approved therapeutics target GPCRs or their direct downstream signaling components.

Many of the GPCR gene mutations identified by the NIH researchers were mutated in a large portion of melanoma patients and already have inhibitors, the most notable being the Glutamate Receptor Metabotropic 3 (GRM3) mutation which could be functionally signification for melanoma tumorigenesis. Therefore, this technology could aid in the development of specific inhibitors of GRM3 as well as the pathway it activates, mitogen-activated protein kinase (MEK), for the treatment of melanoma patients with these mutations. To complement these findings, human melanoma metastatic cell lines harboring GRM3 mutations are also available for licensing.

Potential Commercial Applications:

• Diagnostic array for the detection of GRM3 mutations

• Method of identifying GRM3 inhibitors as therapeutic agents to treat malignant melanoma patients.

• In vitro and in vivo cell model for the GRM3 mutation in melanoma. This is a useful tool for investigating GRM3 phenotype biology, including growth, motility, invasion, and metabolite production.

Competitive Advantages:

• GPCR mutations, GRM3 in particular, are frequent in melanomas.

• Several inhibitors to GPCR and MEK are already in clinical trials, thus this technology may prove useful for the development of novel diagnostic tests and therapeutics.

• Associated cell lines derived from melanoma patients are available.

Development Stage: Pre-clinical

Inventors: Yardena Samuels (NHGRI), Todd Prickett (NHGRI), and Steven Rosenberg (NCI)

Publication: Prickett TD, et al. Exon capture analysis of G-protein coupled receptors reveals activating mutations in GRM3 in melanoma. Nat Genet. 2011 Sep 25;43(11):1119-26. [PMID 21946352]

Intellectual Property:

• HHS Reference No. E-244-2010/0 —U.S. Provisional Application No. 61/462,471 filed 23 Sep 2010; PCT Application No. PCT/US2011/052032 filed 16 Sep 2011

• HHS Reference No. E-029-2012/0 — Research Tool. Patent protection is not being pursued for the GRM3 melanoma metastatic cell lines.

Related Technologies: HHS Reference Nos. — E-013-2011/0 (patent app: PCT); E-024-2012/0 (research tool); E-272-2008/0 (patent app: US, EP); E-229-2010/0 (research tool); E-232-2010/0 (research tool)

Licensing Contact: Whitney Hastings; 301-451-7337; hastingw@mail.nih.gov

Collaborative Research Opportunity: The NHGRI is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this technology. For collaboration opportunities, please contact Claire Driscoll, Director, NHGRI Technology Transfer Office, at cdriscol@mail.nih.gov or 301-594-2235.

Human Melanoma Metastasis Cell Lines Harboring GRM3 Mutations

Description of Technology: Using exon capture and next generation sequencing approaches to analyze the entire G protein coupled receptor (GPCR) gene family in melanoma, the researchers at the NIH have identified several novel somatic (e.g., tumor-specific) alterations. GPCRs play an integral part in regulating physiological functions and the importance of these molecules is evident by the fact that approximately half of the current FDA approved therapeutics target GPCRs or their direct downstream signaling components. Many of the GPCR gene mutations identified by the NIH researchers were mutated in a large portion of melanoma patients and already have inhibitors, the most notable being the Glutamate Receptor Metabotropic 3 (GRM3) mutation which could be functionally signification for melanoma tumorigenesis.

Available for licensing are several melanoma cell lines that harbor GRM3 mutations. These cell lines provide useful and efficient tools for studying melanoma and

can be used in the development of specific inhibitors of GRM3 as well as the pathway it activates, mitogen-activated protein kinase (MEK), for the treatment of melanoma patients with these mutations.

Potential Commercial Applications:

• Diagnostic array for the detection of GRM3 mutations

• Method of identifying GRM3 inhibitors as therapeutic agents to treat malignant melanoma patients.

• In vitro and in vivo cell model for the GRM3 mutation in melanoma. This is a useful tool for investigating GRM3 phenotype biology, including growth, motility, invasion, and metabolite production.

• Tool for testing the activity of GRM3 inhibitors and generating GRM3 mutation knock-outs.

Competitive Advantages:

• Cell lines are derived from melanoma patients

• GRM3 mutations are highly frequent and/or highly mutated in melanomas

• Several inhibitors to GPCR and MEK are already in clinical trials, thus this technology may prove useful for the development of novel diagnostic tests and therapeutics.

Development Stage: Pre-clinical

Inventors: Yardena Samuels (NHGRI), Todd Prickett (NHGRI), and Steven Rosenberg (NCI)

Publication: Prickett TD, et al. Exon capture analysis of G-protein coupled receptors reveals activating mutations in GRM3 in melanoma. Nat Genet. 2011 Sep 25;43(11):1119-26. [PMID 21946352]

Intellectual Property: HHS Reference No. E-029-2012/0 — Research Tool. Patent protection is not being pursued for the GRM3 melanoma metastatic cell lines.

Related Technologies: HHS Reference Nos. — E-244-2010/0 (patent app: PCT); E-013-2011/0 (patent app: PCT); E-024-2012/0 (research tool); E-272-2008/0 (patent app: US, EP); E-229-2010/0 (research tool); E-232-2010/0 (research tool)

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Human Melanoma Metastasis Cell Lines Harboring MITF Mutations

Description of Technology: Researchers at the NIH have found recurrent somatic mutations in the microphthalmia-associated transcription factor (MITF). Previous studies have linked the MITF pathway to the progression of melanoma, however, little is known about somatic gene mutations in the MITF pathway that could contribute to this progression. The NIH researchers evaluated primary and metastatic melanoma samples for the presence of somatic mutations in two genes of the MITF pathway, MITF and SRY (sex determining region Y)-box 10 (SOX10). They identified

16 previously unidentified somatic mutations in these genes. These studies suggest that MITF and SOX10 genes could be used as diagnostic markers in human metastatic melanoma. Consequently, these cell lines could be used to further investigate the effects of MITF and SOX10 in melanoma and to develop therapeutics targeting this gene and protein.

Potential Commercial Applications:

• Diagnostic array for the detection of MITF mutations.

• In vitro and in vivo cell model for the MITF mutations in melanoma. This is a useful tool for investigating MITF phenotype biology, including growth, motility, invasion, and metabolite production.

Competitive Advantages:

• Cell lines are derived from melanoma patients.

• The MITF mutation is frequent in melanomas.

Development Stage: Pre-clinical

Inventors: Yardena Samuels (NHGRI) and Steven Rosenberg (NCI)

Publication: Cronin JC, et al. Frequent mutations in the MITF pathway in melanoma. Pigment Cell Melanoma Res. 2009 Aug;22(4):435-44. [PMID 19422606]

Intellectual Property: HHS Reference No. E-023-2012/0 — Research Tool. Patent protection is not being pursued for the MITF melanoma metastatic cell lines.

Related Technologies: HHS Reference Nos. — E-029-2012/0 (research tool); E-013-2011/0 (patent app: PCT); E-024-2012/0 (research tool); E-272-2008/0 (patent app: US, EP); E-229-2010/0 (research tool); E-232-2010/0 (research tool)

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Human Melanoma Metastasis Cell Lines Harboring TRRAP, GRIN2A, and PLCB4 Mutations

Description of Technology: Researchers at the NIH have identified several novel somatic (e.g., tumor-specific) alterations, many of which have not previously been known to be genetically altered in tumors or linked to melanoma. In particular, the researchers identified a recurrent "hotspot" mutation in the transformation/transcription domain-associated protein (TRRAP) gene, identified the glutamate receptor ionotropic N-methyl D-aspartate 2A (GRIN2A) gene as a highly mutated in melanoma, and have shown that the majority of melanoma tumors have alternations in genes encoding members of the glutamate signaling pathway, such as phospholipase C, beta 4 (PLCB4). Therefore, this technology not only provides a comprehensive map of genetic alterations in melanoma, but has important diagnostic and therapeutic applications.

Available for licensing are several melanoma cell lines that harbor TRRAP, GRIN2A, and PLCB4 mutations. These cell lines provide useful and efficient tools for studying melanoma and can be used in the development of specific therapeutics for patients harboring these mutations. Specifically, these cell lines could be used to develop

inhibitors to limit tumor growth and further understand melanoma and the biology of these genes.

Potential Commercial Applications:

• Diagnostic array for the detection of TRRAP, GRIN2A, and PLCB4 mutations

• Method of identifying TRRAP, GRIN2A, and PLCB4 inhibitors as therapeutic agents to treat malignant melanoma patients.

• In vitro and in vivo cell model for understanding the biology of TRRAP, GRIN2A, and PLCB4, including growth, motility, invasion, and metabolite production.

Competitive Advantages:

• Cell lines are derived from melanoma patients

• TRRAP, GRIN2A, and PLCB4 mutations are highly frequent and/or highly mutated in melanomas

• Glutamate antagonists have already been shown to inhibit tumor growth. Thus, this technology may prove useful for the development of novel diagnostic tests and therapeutics.

Development Stage: Pre-clinical

Inventors: Yardena Samuels (NHGRI) and Steven Rosenberg (NCI)

Publication: Wei X, et al. Exome sequencing identifies GRIN2A as frequently mutated in melanoma. Nat Genet. 2011 May; 43(5):442-6. [PMID 21499247]

Intellectual Property: HHS Reference No. E-024-2012/0 — Research Tool. Patent protection is not being pursued for the TRRAP, GRIN2A, PLCB4 melanoma metastatic cell lines.

Related Technologies: HHS Reference Nos. — E-013-2011/0 (patent apps. PCT); E-272-2008/0 (patent apps. US, EP); E-229-2010/0 (research tool); E-232-2010/0 (research tool); E-029-2012/0 (research tool); E-244-2012/0 (patent app: PCT)

Licensing Contact: Whitney Hastings; 301-451-7337; hastingw@mail.nih.gov

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