

AmbryShare: A Model for Sharing Genomic Data to Understand all Human Disease

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# It's old news; How is AmbryShare different? Let's get personal; Why share genomic data? The challenges ahead; Ok, so what's next?



Excerpt from March 8, 2016 NY Times article:

Charles Dunlop, founder and chief executive of Ambry, said he was approached by drug



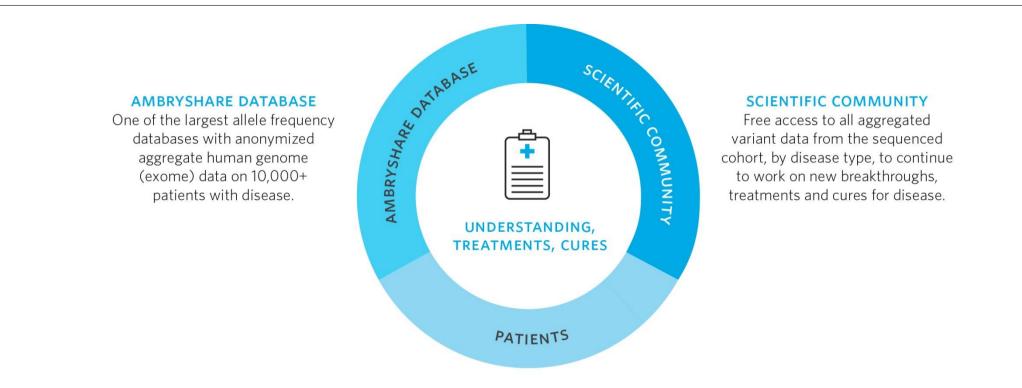
companies, but decided to make the company's data freely available to expedite research.

*"I've got Stage 4 cancer myself," he said, referring to advanced prostate cancer that is in remission. "I don't want to wait an extra day."* 





## The world would be a better place if all human disease was understood.

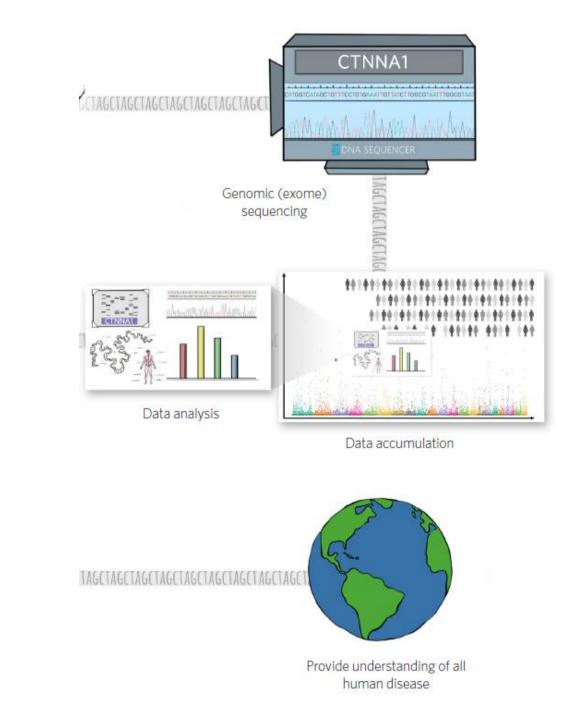


#### PATIENTS

Patients can register with AmbryShare to receive updates, gain access to our family history tool, and take it to their healthcare provider to discuss if genetic counseling and/or testing is right for them.



- A free online genomic database of anonymized aggregated variant allele frequencies from exome sequencing of 10,000+ women with breast and ovarian cancer.
- A plan to expand to many other disease groups and exome sequence hundreds of thousands of individuals with patient engagement in the process.
- AmbryShare is designed to help scientists understand the etiology of disease and identify targeted treatment and disease prevention strategies.
- We hope researchers and pharmaceutical companies worldwide will access this data to accelerate the pace of research.



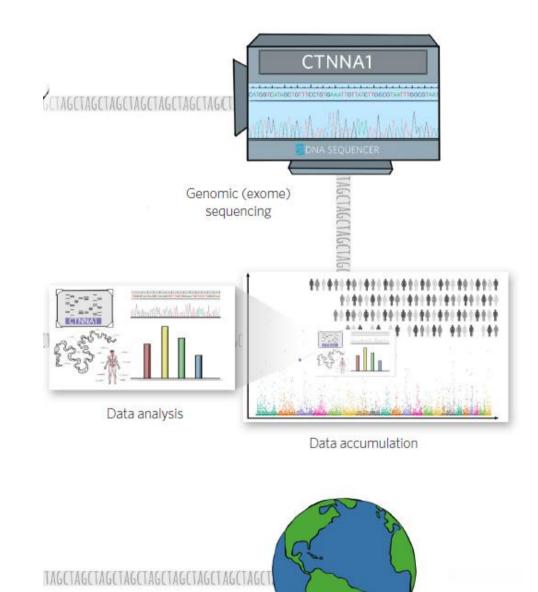
**Ambry Genetics** AmbryShare: How?

## **IRB** Submission

- Deemed EXEMPT from consent requirements under 45 CFR section 46.101(b)(4)
  - "Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects"

#### AmbryShare Cohort Selection

- Samples were selected from patient samples received at Ambry Genetics for clinical genetic testing.
- Patients who declined the use of their sample for research were automatically excluded.
- All patients included in the cohort had a disease and/or diagnosis. The first release was focused on patients diagnosed with breast and/or ovarian cancer.
- Samples were de-identified
- Whole exome sequencing was performed, aggregated, analyzed and deposited online



Provide understanding of all human disease Ambry Genetics | Data at a glimpse

What Type of Information is Available In AmbryShare?

The database provides:

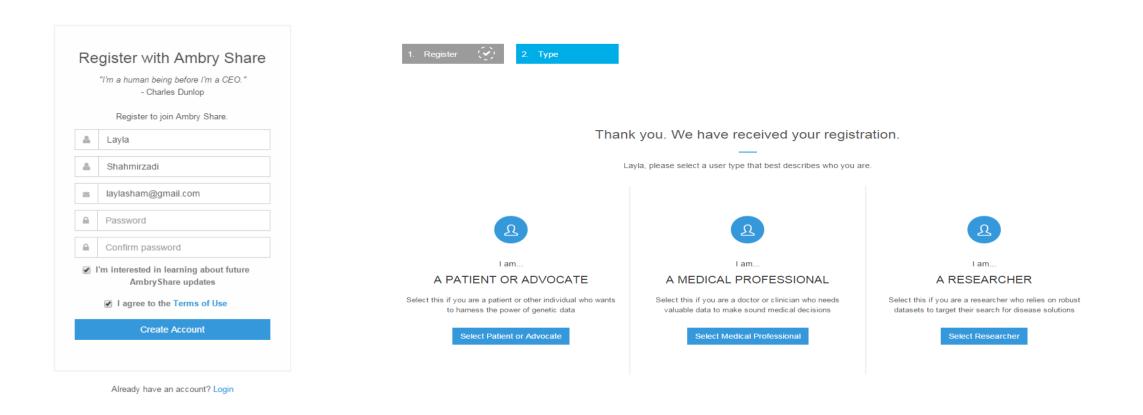
- The disease type (*i.e.* breast cancer)
- Nucleotide alteration
- Protein alteration
- Genomic position
- AmbryShare cohort frequency for each variant observed.
- Information about protein structure and domain organization for each variant.

Overview						
overview						
Gene	TP53 ( 2)					
Descripti	on		Ass	ociated Diseases		
protein is where it&i containing a p53-bind thus funct human ca suppresso but also as variants di	expressed at low level in #39;s believed to contril ; transcription activatior jing site and activate ex, ion as a tumor suppress ncers fail to bind the coi r activity. Alterations of s germline mutations in ue to alternative promo	apoptosis, senescence, DNA repair, or chain normal cells and a ta high level in a variety bute to transformation and malignancy. p53 n, DNA-binding, and oligomerization domain pression of downstream genes that inhibit sor. Mutants of p53 that frequently occur in nsensus DNA binding site, and hence cause this gene occur not only as somatic mutatic some cancer-prone families with Li-Fraume ters and multiple alternative splicing have b an regulate p53 transcriptional activity. [pror	of transformed cell lines, is a DNA-binding protein s. It is postulated to bind to prowth and/or invasion, and a number of different the loss of tumor ns in human malignancies, ni syndrome. Multiple p53 een found. These variants	<ul> <li>Osteosarcoma (OMIM)</li> <li>Nasopharyngeal Carcinoma (OMIM)</li> <li>Li-Fraumeni Syndrome (OMIM)</li> <li>Hepatocellular Carcinoma (OMIM)</li> <li>Glioma Susceptibility 1 (OMIM)</li> <li>Colorectal Cancer (OMIM)</li> <li>Breast Cancer (OMIM)</li> <li>Choroid Plexus Papilloma (OMIM)</li> <li>Basal Cell Carcinoma 7 (OMIM)</li> <li>Adrenal Cortical Carcinoma (OMIM)</li> </ul>		
	rations (257) ClinVar	J				
Number o	rations (257) ClinVar	25 🖸	7) Bratala Alternation	Conomic Bacilian	Ambridbaro Cobort Frequency	Next> La
Number o	rations (257) ClinVar of alterations per page RefSeq ID 6	25 0 Nucleotide Alteration	Protein Alteration	Genomic Position	AmbryShare Cohort Frequency	Next> La
Number of Gene TP53	rations (257) ClinVar of alterations per page RefSeq ID 6 NM_000546	Nucleotide Alteration	Protein Alteration p.P72R	Chr 17:7579472	67.95%	
Number o	rations (257) ClinVar of alterations per page RefSeq ID 6	22 C Nucleotide Alteration ( c.215C>G c.74+38C>G				
Gene TP53 TP53	RefSeq ID     6       NM_000546     NM_000546	Nucleotide Alteration		Chr 17:7579472 Chr 17:7579801	67.95% 61.83%	
Gene TP53 TP53 TP53	RefSeq ID     6       NM_000546     NM_000546       NM_000546     NM_000546	25     3       Nucleotide Alteration     (       c.215C-G     (       c.74+38C>G     (       c.96+41_97-54DEL16     (		Chr 17:7579472 Chr 17:7579801 Chr 17:7579644	67.95% 61.83% 52.52%	
Gene           TP53           TP53           TP53	RefSeq ID     6       NM_000546     NM_000546       NM_000546     NM_000546	23     3       Nucleotide Alteration     ()       c.215C>G     ()       c.74+38C>G     ()       c.96+41_97-54DEL16     ()       c.376-91G>A		Chr 17:7579472 Chr 17:7579801 Chr 17:7579644 Chr 17:7578645	67.95% 61.83% 52.52% 49.92%	
Gene           TP53           TP53           TP53           TP53           TP53           TP53	Refseq ID         6           NM_000546         NM_000546           NM_000546         NM_000546           NM_000546         NM_000546	25     C       Nucleotide Alteration     C       c.215C>G     C       c.74+38C>G     C       c.96+41_97-54DEL16     C       c.376-91G>A     C       c.672+62A>G     C		Chr 17:7579472 Chr 17:7579801 Chr 17:7579644 Chr 17:7578645 Chr 17:7578115	67.95% 61.83% 52.52% 49.92% 21.61%	
Gene           7P53           7P53           7P53           7P53           7P53           7P53	RefSeq ID         6           NM_000546         NM_000546           NM_000546         NM_000546           NM_000546         NM_000546           NM_000546         NM_000546	25     Comparison       Nucleotide Alteration     Caltocode       c.215C>G     Caltocode       c.74+38C>G     Caltocode       c.96+41_97-54DEL16     Caltocode       c.376-91G>A     Caltocode       c.572+62A>G     Caltocode       c.97-29C>A     Caltocode		Chr 17:7579472           Chr 17:7579801           Chr 17:7579644           Chr 17:7578645           Chr 17:7578115           Chr 17:7579619	67.95%       61.83%       52.52%       49.92%       21.61%       4.27%	
Gene           TP53           TP53           TP53           TP53           TP53           TP53           TP53           TP53           TP53           TP53	RefSeq ID         6           NM_000546         NM_000546           NM_000546         NM_000546           NM_000546         NM_000546           NM_000546         NM_000546           NM_000546         NM_000546           NM_000546         NM_000546	25         Nucleotide Alteration           c.215C>G         c.215C>G           c.74+38C>G         c.74+38C>G           c.96+41-97-54DEL16         c.376-91G>A           c.372+62A>G         c.97-29C>A           c.376-100_376-158DELAAA         c.376-100_376-158DELAAA	p,P72R	Chr 17:7579472           Chr 17:7579801           Chr 17:7579644           Chr 17:7576645           Chr 17:7578615           Chr 17:7579619           Chr 17:7578712	67.95%       61.83%       52.52%       49.92%       21.61%       4.27%       3.96%	

- ① Search by gene/alteration
- ② Gene description
- 3 Associated diseases
- ④ Total number of alterations identified

- **(5)** Link out to ClinVar
- 6 RefSeq ID
- ⑦ Nucleotide and protein alterations
  - Allele frequency among AmbryShare cohort

# **Ambry Genetics** More about the Database: Register with AmbryShare



https://share.ambrygen.com/terms-of-use

**Ambry Genetics** What Are the Future Plans for AmbryShare?

- Continue to add patients and many diseases to the database
- IRB approval for permission to re-contact
- Expanded patient Involvement
- Worldwide research collaborations

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Neurodevelopmental Disorders >	and a second s		



#### Get to Know Ambry Genetics

Ambry Genetics is a privately-held healthcare company with the most comprehensive suite of genetic testing solutions for inherited and non-inherited diseases. Since 1999, Ambry has tested nearly one million patient samples benefiting 94% of all U.S. patients covered by public and private insurers. Ambry is dedicated to scientific collaboration by offering its rapidly growing database of anonymized genomic data (variant frequencies) free to the global medical research community to fulfill the promise of the human genome to cure or manage all human disease. Ambry is dedicated to the belief that human health should not be patented or owned, and genomic data should be freely shared so we can try to understand all human disease.



For more information on collaboration with AmbryShare, contact us at share@ambrygen.com

