Screen all your COPD patients with

AlphaID™

Cheek Swab Dried Blood Spot

AlphaID provides *completely free* screening for alpha$_1$-antitrypsin deficiency (alpha-1)

Alpha-1 is the #1 known genetic risk factor for COPD[1]

GRIFOLS

Alpha-1 is the #1 Known Genetic Risk Factor for COPD[1]

Alpha-1 may be a contributing cause in **up to 3% of COPD cases** in the United States—**up to 300,000 people**[1]

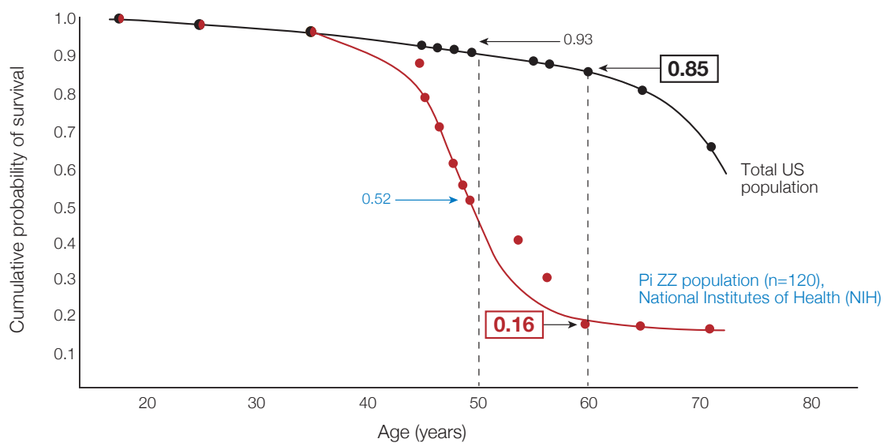
First described in 1963, alpha-1 is **caused by a mutation** of the SERPINA1 gene located on chromosome 14[2]

Alpha1-antitrypsin protects the lungs from proteolytic attack, particularly by neutrophil elastase. Without sufficient levels of alpha1-antitrypsin, lung damage occurs[1]

A landmark study indicated that **severe alpha-1 significantly shortened life span**[2]

- Mean survival of the alpha-1 cohort (n=120) was 16% at 60 years of age, compared with 85% for the general population

Survival analysis of severely deficient alpha-1 individuals vs total US population[2]*



Study Design, 1988: All 120 Pi ZZ subjects evaluated as inpatients in NIH Clinical Center. Various demographic features, clinical findings, and electrocardiogram evaluations were obtained from medical records. Blood and urine laboratory findings were obtained through computerized archives of the Clinical Center Laboratories. Chest radiographs and scintigraphic scans were evaluated de novo at the time of this analysis, with knowledge of the diagnosis but without knowledge of any of the other data. Lung function tests were obtained from the computerized files of the Pulmonary Branch. Mortality data were obtained at the time of this analysis. Alpha$_1$-antitrypsin protein phenotypes were determined by a combination of isoelectric focusing of serum, quantitation of AAT levels in serum, and family studies.[2]

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Alpha-1 is Underdiagnosed[1]

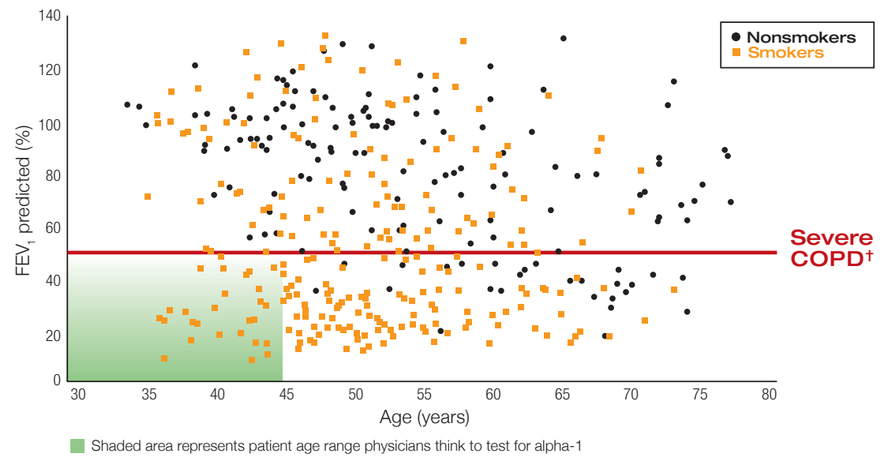
More than 90% of people with alpha-1 are estimated to be undiagnosed

The **average delay** between the onset of symptoms and diagnosis of alpha-1 is **8.3 years**

The average **number of physicians** seen before being correctly diagnosed is **2.7**

Alpha-1 occurs in both nonsmokers and smokers

FEV$_1$ percentage predicted by age and distinguished by smoking status[1,3]*



*378 Pi ZZ patients.

†Stage III severe COPD, GOLD guidelines.

These Major Respiratory Organizations Recommend Targeted Genetic Screening for Alpha-1 in All Patients With COPD[4-8]

ATS: American Thoracic Society

CHEST: American College of Chest Physicians

COPD Foundation: Chronic Obstructive Pulmonary Disease

GOLD: Global Initiative for Chronic Obstructive Lung Disease

WHO: World Health Organization

The American Thoracic Society recommends screening for alpha-1 regardless of age, smoking history, or FEV_1 in[4]:

- **All adults with symptomatic COPD or asthma**
- **All adults with symptomatic asthma** whose airflow obstruction is incompletely reversible after bronchodilator therapy
- **Asymptomatic patients with persistent obstruction** on pulmonary function tests and with identifiable risk factors (eg, smoking, occupational exposure)
- **All immediate family members** of patients who are diagnosed with alpha-1

Screening patients with COPD for alpha-1:

- Identifies those with a severe alpha-1 for whom treatment may be appropriate[4]
- Identifies carriers of deficient alleles, which can be passed onto children[1]
- Provides incentive for smoking cessation[9]
  - In a follow-up study, 59% of patients with severe alpha-1 attempted to quit smoking after receiving test results and minimal counseling

Use AlphaID to Screen for Alpha-1

Each sample is processed by Biocerna, a **CLIA-certified**, independent laboratory and **analyzed by alpha-1 experts**[10]

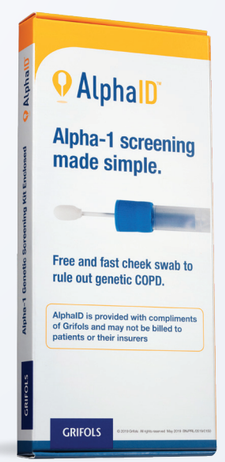
Comprehensive results are available within **3-5 days** from the time the sample is returned to the laboratory[10]

- Results are accessible through the confidential, easy-to-use portal at **myalphaID.com.** Ordering clinicians may contact **alphaid@biocerna.com** to add additional staff to the portal
- Results are also received by fax

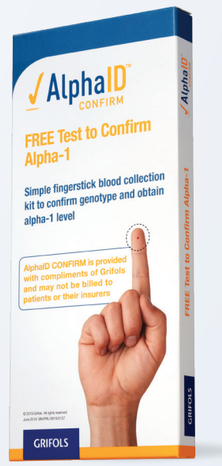
Alpha-1 expert clinicians are available for **personal consultation to discuss abnormal results**

Results are **strictly confidential** and are shared only with the ordering clinician and designated office staff

There is **NO COST** for the screening. AlphaID is provided compliments of Grifols and may not be billed to patients or their insurers



Cheek Swab



Dried Blood Spot

AlphaID™

A free, fast, and easy way to rule out alpha-1

	AlphaID:
Fast	A gentle cheek swab that only takes seconds. There are no chemicals to add and no cards to dry
Familiar	Uses the same DNA collection and screening methods as many at-home genetic testing kits
Reliable	Delivers accurate and reliable genotyping results[11]
Specific	Screens for the 14 most-prevalent mutations associated with alpha-1, including S, Z, F, I, rare, and null alleles[11]
Confidential	Results are available only to the ordering clinician and designated office staff
Completely Free	Provided compliments of Grifols and may not be billed to patients or their insurers

The AlphaID kit contains everything you need to collect and submit a cheek swab sample for alpha-1 screening

- Instructions
- Requisition form
- Cheek swab
- Specimen bag
- Mailer box
- Prepaid shipping label

EXAMPLE RESULTS REPORT

FINAL

biocerna

Biocerna
8161 Maple Lawn Blvd Ste 375
Fulton, MD 20759
Phone: 1-855-DNA-LAB1 (855-362-5221)
Fax: 301-769-6659

CLIA ID#: 21D2059950
MD State License#: 2007
CAP Accr. #:874287701
Lab Director:
Tammey Naab, MD

Patient:	Patient, B			Accession:	19162
Doctor:	Grifols, Test	Birth:	2/2/1945		
		Age:	74 years	Collection Date:	12/1/2019 12:58 PM
		Gender:	Male	Received Date:	12/4/2019 12:58 PM EF
				Requisition Barcode#	123456

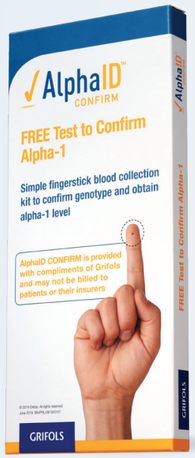
Test Name	Flag	Result	Units	Reference Range/Cutoff
A1AT Genetic Testing				*Run by EF on 12/4/2019 1:12:14 PM at Location: 1*
A1AT Genotype	**ABNORMAL**	ZZ		(NORMAL REFERENCE=M/M)

AlphaID Specimen Type: Saliva from DNA Genotek Oracollect Dx OCD-100 swab.

AlphaID reports the alpha-1 genotype. Any result other than a homozygous MM is considered abnormal.[3]

AlphaID™ CONFIRM

Confirming an alpha-1 diagnosis is simple



	AlphaID CONFIRM:
Efficient	Uses a dried blood spot card to screen for alpha-1 or confirm the results from an AlphaID cheek swab
Comprehensive	Confirms alpha-1 genotype and reports the serum level of alpha$_1$-antitrypsin
Reliable	Delivers accurate and reliable genotyping results[11]
Specific	Screens for the 14 most-prevalent mutations associated with alpha-1, including S, Z, F, I, rare, and null alleles[11]
Confidential	Results are available only to the ordering clinician and designated office staff
Completely Free	Provided compliments of Grifols and may not be billed to patients or their insurers

The AlphaID CONFIRM kit contains everything you need to collect and submit a dried blood sample for alpha-1 screening

- Instructions
- Requisition form
- Two lancets
- Alcohol pads, gauze, and bandage
- Dried blood spot card
- Postage-paid envelope

EXAMPLE RESULTS REPORT

FINAL

Biocerna
8161 Maple Lawn Blvd Ste 375
Fulton, MD 20759
Phone: 1-855-DNA-LAB1 (855-362-5221)
Fax: 301-769-6659

CLIA ID#: 21D2059950
MD State License#: 2007
CAP Accr. #:874287701
Lab Director:
Tammey Naab, MD

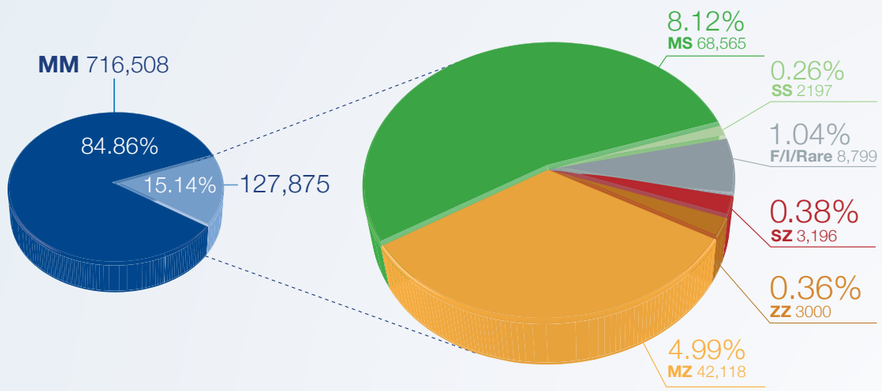
Patient:	Patient , F			Accession:	19168
Doctor:	Grifols, Test	Birth:	5/25/1965		
		Age:	54 years	Collection Date:	12/1/2019 1:00 PM
		Gender:	Female	Received Date:	12/4/2019 1:00 PM EF
				Requisition Barcode#	123456

Test Name	Flag	Result	Units	Reference Range/Cutoff
Alpha-1 Antitrypsin Immunoassay				*Run by CLS on 12/4/2019 2:37:55 PM at Location: 1*
Alpha-1 Antitrypsin	**ABNORMAL**	44.6	mg/dL	90.0 - 200.0
AlphaID CONFIRM - A1AT Genetic Testing				*Run by EF on 12/4/2019 1:17:47 PM at Location: 1*
A1AT Genotype	**ABNORMAL**	Z/Z		(NORMAL REFERENCE=M/M)

AlphaID CONFIRM reports the alpha-1 genotype as well as the alpha$_1$-antitrypsin level (normal is 90.0 to 200.0 mg/dL).

Abnormal Alpha-1 Alleles Are Common[10]

Among the more than 800,000 patients screened for alpha-1 in the past 10 years, 15% (over 125,000 patients) had at least one deficient allele[10]

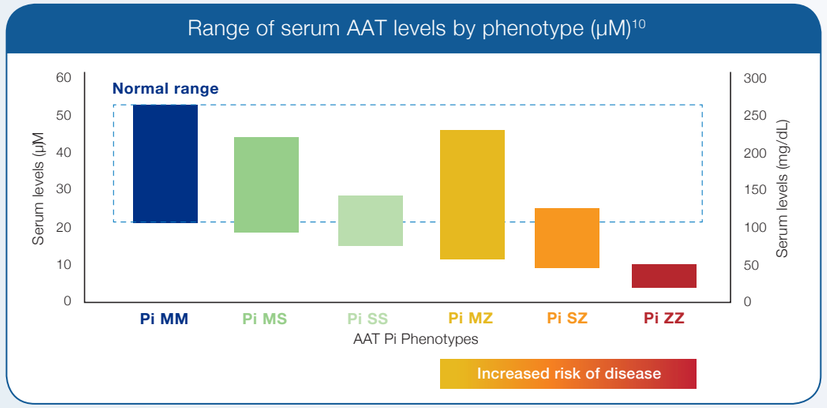


AlphaID and AlphaID CONFIRM detect 14 genetic variations associated with alpha-1[11]

- **Most common normal allele:** M
- **Most common deficient alleles:** S, Z, F, I
- **Less common deficient alleles:** P Lowell, Y Barcelona, M Procida, M Malton, S Iiyama, M Heerlen
- **Null alleles:** Q0 Granite Falls, Q0 West, Q0 Bellingham, Q0 Mattawa, Q0 Ourem, Q0 Clayton

Since adding F and I into screening in 2014, we've found them at a rate of 0.91%.

All deficient alleles compromise alpha$_1$-antitrypsin production, but the effect is most pronounced for the Z allele[10]

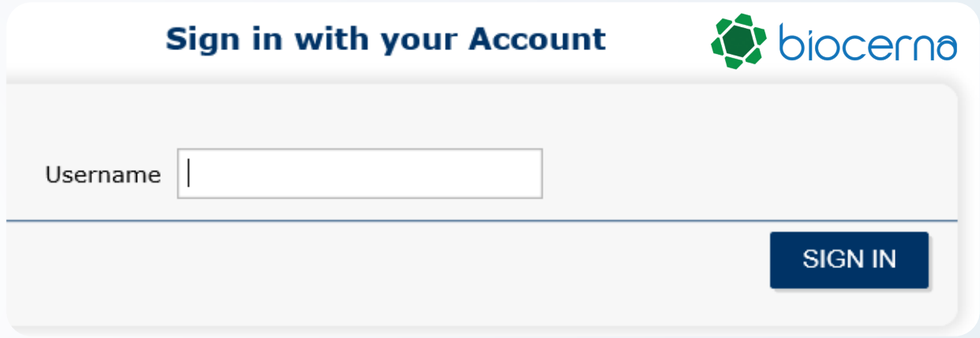


The My AlphaID Portal is a Convenient Way to Manage Alpha-1 Results for All of Your Patients

AlphaID kits are processed by the Alpha-1 Antitrypsin Laboratory at Biocerna

My AlphaID Portal access is granted by following this 3-step process:

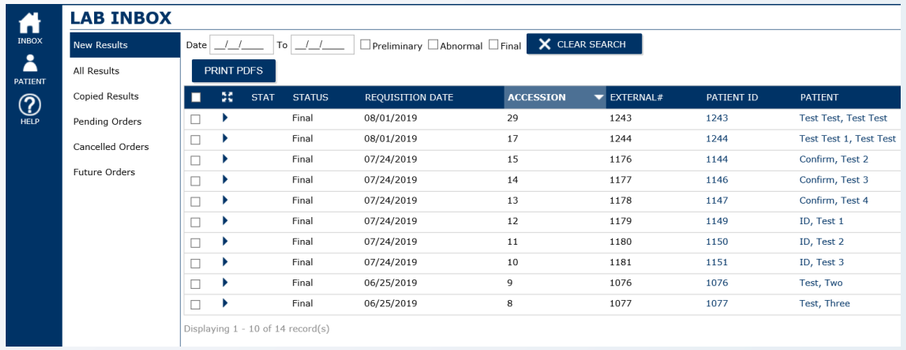
1. Provide your email address on the AlphaID requisition form
2. You will receive an email that the account is active and to change your password
3. Sign in with your account, change password, and access patient results



My AlphaID Portal provides:

- Convenient Management
- Timely Results
- Comprehensive Reporting
- Staff Access

Access confidential results processed by a certified, independent laboratory



First time users can also contact alphaid@biocerna.com for access to your account

Use AlphaID to Screen Appropriate Patients for Alpha-1

- AlphaID provides **completely free** screening for alpha$_1$-antitrypsin deficiency (alpha-1), the #1 known genetic risk factor for COPD[1]
- More than 90% of people with alpha-1 are estimated to be undiagnosed[1]
- Major respiratory organizations recommend targeted genetic screening for alpha-1 in all patients with COPD[4-8]
- **AlphaID and AlphaID CONFIRM kits contain everything you need to screen for alpha-1**

Grifols is Committed to Supporting Patients with Alpha-1

Grifols is dedicated to advancing the understanding of alpha-1. Grifols has been the leader in alpha-1 screening for more than 20 years and continues to develop innovative ways to screen patients.

To begin screening with **AlphaID**,
call your sales representative or visit **RequestAlphaID.com**

References: 1. Campos MA, Wanner A, Zhang G, Sandhaus RA. Trends in the diagnosis of symptomatic patients with α1-antitrypsin deficiency between 1968 and 2003. *Chest.* 2005;128(3):1179-1186. **2.** Brantly ML, Paul LD, Miller BH, Falk RT, Wu M, Crystal RG. Clinical features and history of the destructive lung disease associated with alpha-1-antitrypsin deficiency of adults with pulmonary symptoms. *Am Rev Respir Dis.* 1988;138(2):327-336. **3.** de Serres FJ, Blanco I, Fernández-Bustillo E. Genetic epidemiology of alpha-1 antitrypsin deficiency in North America and Australia/New Zealand: Australia, Canada, New Zealand and the United States of America. *Clin Genet.* 2003;64(5):382-397. **4.** American Thoracic Society/European Respiratory Society. American Thoracic Society/European Respiratory Society statement: Standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. *Am J Respir Crit Care Med.* 2003;168(7):818-900. **5.** CHEST Foundation. Learn About Alpha-1 Antitrypsin Deficiency. https://foundation.chestnet.org/patient-education-resources/alpha-1-antitrypsin-deficiency/. Last reviewed January 2019. Accessed March 6, 2020. **6.** Sandhaus RA, Turino G, Brantly ML, et al. The diagnosis and management of alpha$_1$-antitrypsin deficiency in the adult. *Chronic Obstr Pulm Dis.* 2016;3(3):668-682. **7.** Global Initiative for Chronic Obstructive Lung Disease. *Pocket Guide to COPD Diagnosis, Management, and Prevention: 2020 Report.* 2020:1-57. **8.** World Health Organization. Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach. 2017. https://www. who.int/gard/publications/GARD_Manual/en/. Accessed March 6, 2020. **9.** Carpenter MJ, Strange C, Jones Y, et al. Does genetic testing result in behavioral health change? Changes in smoking behavior following testing for alpha-1 antitrypsin deficiency. *Ann Behav Med.* 2007;33(1):22-28. **10.** Data on file, Alpha-1 Genetics Laboratory. **11.** A1AT Genotyping Test [510(k) Summary]. Bizkaia, Spain: Progenika Biopharma.

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