UNDERSTANDING
TRK FUSION CANCER

TRK, tropomyosin receptor kinase.

GENOMICS AND CANCER

The Role of Genes in Cancer

- Damage or changes to our genes can cause cancer cells to grow and eventually form a tumor[1]

Looking Deeper Into the Cause

- The science of understanding genes and how they relate to diseases is called genomics[2,3]

Precision Medicine

- Precision medicine (also called personalized medicine) aims to prevent, diagnose, and treat disease based on a person's unique health profile, which includes their genomics[2,4-6]

Genomic Cancer Testing Versus Genetic Testing

- Genomic cancer testing is a special kind of testing to find out which gene changes may be triggering the cancer. It can help doctors match patients to an appropriate treatment or clinical trial[3,7]
- Genetic testing looks at a person's unique genetic profile (which is passed down from parents to child) to understand their inherited risk for getting cancer[8]

References: 1. National Cancer Institute. https://www.cancer.gov/about-cancer/causes-prevention/genetics. Accessed April 1, 2019. **2.** National Institute of Health. https://ghr.nlm.nih.gov/primer/precisionmedicine/definition. Published January 15, 2019. Accessed April 1, 2019. **3.** Vaishnavi A, Le AT, Doebele RC. *Cancer Discov*. 2015;5(1):25-34. **4.** Verma M. *J Pers Med*. 2012;2:1-14. **5.** Boland GM, Piha-Paul SA, Subbiah V, et al. *Oncotarget*. 2015;6(24):20099-20110. **6.** Yates LR, Seoane J, Le Tourneau C, et al. *Ann Oncol*. 2018;29(1):30-35. **7.** Foundation Medicine. https://www.foundationmedicine.com/genomic-testing. Accessed March 28, 2019. **8.** American Cancer Society. https://www.cancer.org/cancer/cancer-causes/genetics/understanding-genetic-testing-for-cancer.html. Accessed May 17, 2019.

PRECISION MEDICINE USES THE UNIQUE PROFILE OF A TUMOR TO DEFINE YOUR TREATMENT JOURNEY[1-3]

Traditional cancer diagnosis[4,5]

Cancer diagnosis using precision medicine[1,4]

Your doctor will discuss your health and determine what tests are necessary[5]

Blood tests are usually ordered, since they can detect substances that may be linked with cancer[5]

X-rays, ultrasound, CT scans, and MRIs are often used to help see inside your body[5]

Your doctor might also want to take a tissue sample to examine it more closely[5]

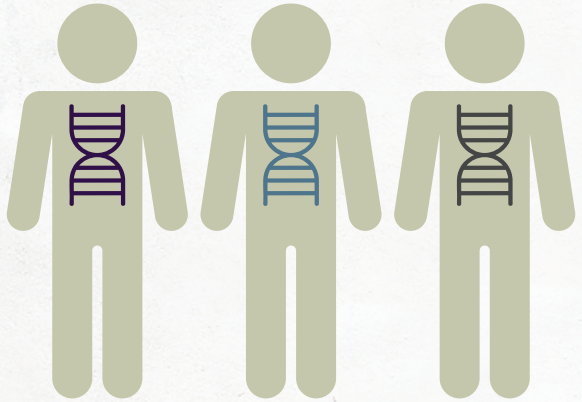
A tissue or blood sample is tested to learn which genomic alteration may be driving the cancer[6,7]

Common Factors Influencing Treatment Selection

- Cancer stage
- Tumor characteristics
- Other medical conditions
- Patient preference
- **Molecular/genomic characteristics**

References: 1. Verma M. *J Pers Med*. 2012;2:1-14. **2.** Boland GM, Piha-Paul SA, Subbiah V, et al. *Oncotarget*. 2015;6(24):20099-20110. **3.** Yates LR, Seoane J, Le Tourneau C, et al. *Ann Oncol*. 2018;29(1):30-35. **4.** American Cancer Society. https://www.cancer.org/cancer/non-small-cell-lung-cancer/detection-diagnosis-staging.html. Accessed June 5, 2019. **5.** National Cancer Institute. https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis. Published March 9, 2015. Accessed June 5, 2019. **6.** American Cancer Society. https://www.cancer.org/cancer/cancer-causes/genetics/genes-and-cancer/genes-in-cancer-diagnosis-and-treatment.html. Accessed June 5, 2019. **7.** Foundation Medicine. https://www.foundationmedicine.com/genomic-testing. Accessed March 28, 2019.

DIAGNOSING AND TREATING CANCER WITH GENOMIC PROFILING



- Genomic profiling requires specialized testing (called genomic cancer testing) to find changes known as genomic alterations. Some of these genomic alterations can help doctors make treatment decisions[1]
- Many patients who get genomic profiling may discover they have a genomic alteration that can be matched to an approved treatment or clinical trial[2-4]

Normal genes (without alterations) provide instructions on how to make proteins and other molecules needed for the body to function properly[5]

***NTRK* gene fusion is a genomic alteration that can help doctors make treatment decisions.**[1,6]

References: 1. Vaishnavi A, Le AT, Doebele RC. *Cancer Discov*. 2015;5(1):25-34. **2.** Boland GM, Piha-Paul SA, Subbiah V, et al. *Oncotarget*. 2015;6(24):20099-20110. **3.** Massard C, Michiels S, Ferté C, et al. *Cancer Discov*. 2017;7(6):586-595. **4.** Harris MH, DuBois SG, Glade Bender JL, et al. *JAMA Oncol*. 2016;2(5):608-615. **5.** National Institutes of Health. https://ghr.nlm.nih.gov/primer/howgeneswork/makingprotein. Accessed June 26, 2019. **6.** Amatu A, Sartore-Bianchi A, Siena S. *ESMO Open*. 2016;1(2):e000023.

HOW GENOMIC CANCER TESTING CAN UNCOVER *NTRK* GENE FUSIONS AND OTHER GENOMIC ALTERATIONS

- Genomic cancer testing lets us look closer at the genes that make up a tumor[1]
- Using a tissue or blood sample, a lab pathologist can identify genomic alterations that may be causing cancer[1]
- This process can identify abnormalities, such as *NTRK* gene fusions, that may be matched with approved or investigational treatments[1,2]
- Not all genomic alterations are treatable. It is important to talk with your doctor about the results of your test and if you are eligible for any approved treatments

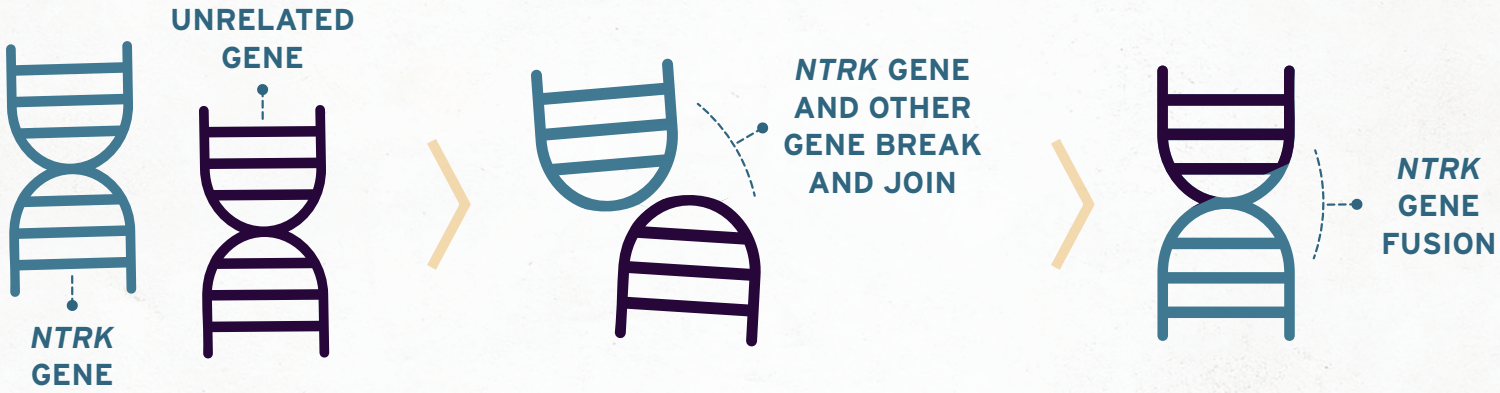
The only way to find *NTRK* gene fusion is to properly test for it.[3]

References: 1. Foundation Medicine. https://www.foundationmedicine.com/genomic-testing. Accessed March 28, 2019. **2.** Vaishnavi A, Le AT, Doebele RC. *Cancer Discov.* 2015;5(1):25-34. **3.** Murphy DA, Ely HA, Shoemaker R, et al. *Appl Immunohistochem Mol Morphol.* 2017;25:513-523.

WHAT IS TRK FUSION CANCER?

- **TRK fusion cancer** is a type of cancer caused by a change to one of our genes, called *NTRK*. This change is called *NTRK* gene fusion[1-3]
- *NTRK* gene fusion occurs when an *NTRK* gene joins together, or fuses, with a different gene. This creates and activates TRK fusion proteins[1-3]
- These proteins can cause cancer cells to multiply and form a tumor[1-3]

NTRK gene fusion[1-3]



References: 1. Amatu A, Sartore-Bianchi A, Siena S. *ESMO Open*. 2016;1(2):e000023. **2.** Kumar-Sinha C, Kalyana-Sundaram S, Chinnaiyan AM. *Genome Med*. 2015;7:129. doi:10.1186/s13073-015-0252-1. **3.** Mertens F, Antonescu CR, Mitelman F. *Genes Chromosomes Cancer*. 2016;55(4):291-310.

TRK FUSION CANCER CAN OCCUR IN DIFFERENT TUMOR TYPES[1-3]

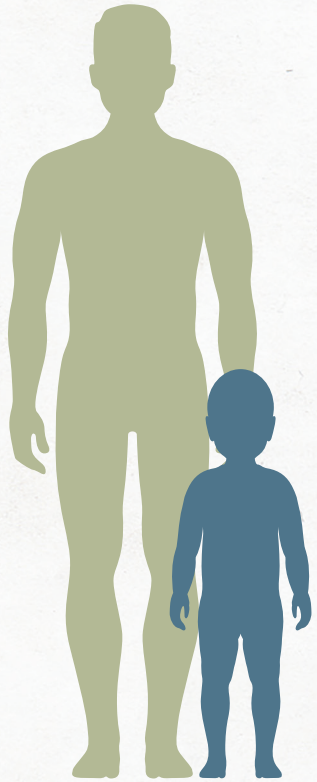
- **TRK fusion cancer** is caused by *NTRK* gene fusion[1]
- *NTRK* gene fusion can occur in many different common and rare tumor types[1-3]

Common Types of Cancer That Can Be Caused by *NTRK* Gene Fusion[1-2]

- Colon
- Kidney
- Liver
- Lung
- Skin
- Thyroid
- And others

Rare Types of Cancer That Can Be Caused by *NTRK* Gene Fusion[1-2]

- Appendix
- Brain
- Secretory breast cancer
- Head and neck
- Salivary gland
- Soft tissue sarcoma
- Infantile fibrosarcoma (pediatric)
- Congenital mesoblastic nephroma (pediatric)



References: 1. Vaishnavi A, Le AT, Doebele RC. *Cancer Discov*. 2015;5(1):25-34. **2.** Amatu A, Sartore-Bianchi A, Siena S. *ESMO Open*. 2016;1(2):e000023. **3.** Li Z, Beutel G, Rhein M, et al. *Blood*. 2009;113(9):2028-2037.

GETTING TESTED FOR TRK FUSION CANCER

There Are Several Different Ways to Test for TRK Fusion Cancer

- **Next-generation sequencing (NGS)** is considered to be the most complete genomic cancer test. This means that it can detect many genomic alterations at once, rather than one at a time. In some cases, your doctor must request that *NTRK* gene fusions (involving the genes *NTRK1*, *NTRK2*, or *NTRK3*) are included[1-3]
- **Immunohistochemistry (IHC)** is a "staining" technique, a way for doctors and scientists to better see and classify cells under a microscope. IHC uses special proteins known as antibodies to identify the type of cancer. These antibodies will attach only to specific molecules on certain cancer cells, revealing a color change[4,5]
- **Fluorescence in-situ hybridization (FISH)** is a test where chromosomes are vividly painted with fluorescent molecules. This helps the doctor see changes that can cause tumors to form and grow. In this test, one alteration lights up at a time[6]
- **Reverse-transcriptase polymerase chain reaction (RT-PCR)** is a multistep process that uses many copies of a specific DNA segment to find changes in a gene. This process can only detect a limited number of alterations at once[5,7]

Each test has its own benefits and limitations. Ask your doctor what type of testing is right for you.

References: 1. Su D, Zhang D, Chen K, et al. *J Exp Clin Cancer Res*. 2017;36(1):121. **2.** Lih CJ, Harrington RD, Sims DJ, et al. *J Mol Diagn*. 2017;19(2):313-327. **3.** Rogers T-M, Arnau GM, Ryland GL, et al. *Sci Rep*. 2017;7:42259. doi:10.1038/srep42259. **4.** American Cancer Society. https://www.cancer.org/cancer/non-small-cell-lung-cancer/detection-diagnosis-staging.html. Accessed June 5, 2019. **5.** National Cancer Institute. https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis/pathology-reports-fact-sheet. Accessed June 25, 2019. **6.** Cui C, Shu W, Li P. *Front Cell Dev Biol*. 2016;4:89. **7.** Abel HJ, Al-Kateb H, Cottrell CE, et al. *J Mol Diagn*. 2014;16(4):405-417.

TALK TO YOUR DOCTOR ABOUT TESTING

Some Questions You May Want to Ask

- Have I had genomic cancer testing?
- If so, when? What information did it provide about my cancer? Did the test include *NTRK* gene fusions?
- If not, would genomic cancer testing help us learn more about my tumor?

The good news is, we are learning more about cancer every day. Genomic cancer testing can help your doctor offer you a more individualized treatment plan that's right for you. **Even if you were diagnosed long ago, ask your doctor whether genomic cancer testing could help guide your treatment decisions, now or in the future.** Ask your doctor which type of testing is best for you.

RESOURCES FOR YOU, YOUR FAMILY, OR CAREGIVERS

TRKcancer.com

- Provides more information about TRK fusion cancer, plus a downloadable checklist to share with your doctor

testyourcancer.com

- Offers more knowledge about genomic cancer testing

WHAT YOU SHOULD KNOW

- Cancer is caused by damaged or changed genes[1]
- Precision medicine is a more personalized approach to help guide cancer care[2,3]
- Some patients who get genomic profiling may discover they have a genomic alteration that is linked to an approved or investigational treatment[4-6]
- Genomic cancer testing can uncover *NTRK* gene fusions and other genomic alterations[7,8]
- TRK fusion cancer is a type of cancer caused by a change to the *NTRK* gene[9-11]
- TRK fusion cancer can occur in both rare and common tumor types, in adults and children[3,9]

If you have questions about TRK fusion cancer or genomic testing, speak to your healthcare provider or visit TRKcancer.com.

References: 1. NIH-National Cancer Institute. https://www.cancer.gov/about-cancer/causes-prevention/genetics. Accessed March 26, 2019. **2.** US National Library of Medicine. Genetics Home Reference. https://ghr.nlm.nih.gov/primer/precisionmedicine/definition. Published January 15, 2019. Accessed April 1, 2019. **3.** Vaishnavi A, Le AT, Doebele RC. *Cancer Discov.* 2015;5(1):25-34. **4.** Boland GM, Piha-Paul SA, Subbiah V, et al. *Oncotarget*. 2015;6(24):20099-20110. **5.** Massard C, Michiels S, Ferté C, et al. *Cancer Discov.* 2017;7(6):586-595. **6.** Harris MH, DuBois SG, Glade Bender JL, et al. *JAMA Oncol.* 2016;2(5):608-615. **7.** Foundation Medicine. https://www.foundationmedicine.com/genomic-testing. Accessed March 28, 2019. **8.** Murphy DA, Ely HA, Shoemaker R, et al. *Appl Immunohistochem Mol Morphol*. 2017;25:513-523. **9.** Amatu A, Sartore-Bianchi A, Siena S. *ESMO Open*. 2016;1(2):e000023. **10.** Kumar-Sinha C, Kalyana-Sundaram S, Chinnaiyan AM. *Genome Med*. 2015;7:129. doi:10.1186/s13073-015-0252-1. **11.** Mertens F, Antonescu CR, Mitelman F. *Genes Chromosomes Cancer*. 2016;55(4):291-310.

PP-PF-ONC-ALL-0091-1 08/2019