AWMGS
All Wales Medical Genomics Service

Lynch Syndrome Genomic Testing (R210)
Patient Information Leaflet

You have been given this leaflet following your diagnosis of bowel cancer. In Wales tumour testing is routinely completed on bowel cancer biopsies to investigate whether a cancer could be due to an inherited genetic condition. Tests were done on your tumour, which indicated this could be the case.

There are two possible reasons for these results. One possibility is that this is caused by a sporadic DNA change that is only present in tumour cells. Alternatively, there is a chance that you may have inherited a condition called Lynch Syndrome (LS), which could have been passed on to others in the family. Evidence has shown that ~50% of people with these tumour testing results are diagnosed with LS. Therefore, we can offer you genetic testing to clarify your status.

Lynch syndrome (LS)

LS is an inherited cancer condition which is associated with an increased risk of developing certain types of cancer including bowel cancer and endometrial (womb) cancer for women. Men and women with LS are also at increased risk of developing several other different types of cancers, including ovarian, stomach, small bowel, liver, bile duct, upper urinary tract, prostate, brain and skin cancers. It is important to remember however that a diagnosis of LS only makes an individual predisposed to developing cancer, and some people with LS will never go on to develop cancer. Further information about Lynch syndrome is available through the Lynch Syndrome UK webpage: https://www.lynch-syndrome-uk.org

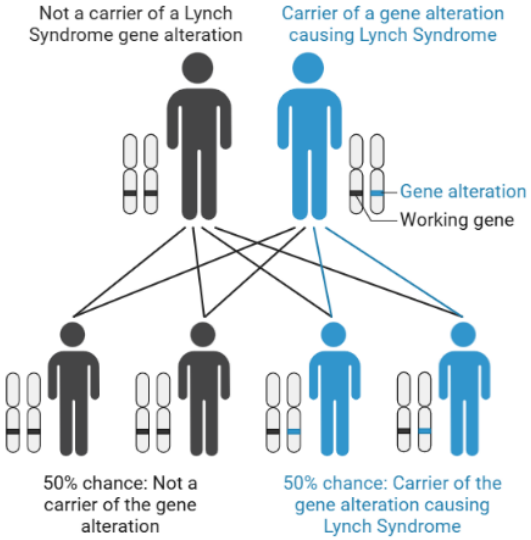
Genes and DNA

DNA is present in most cells and carries our unique genetic information. We each have tens of thousands of genes, which act as our body's instruction book. Our genes tell our body to work, grow, develop and function. Some genes offer us protection from cancer, by repairing errors that occur when cells are dividing such as the MMR genes. We are currently aware of the MMR genes; MLH1, MSH2, EPCAM, MSH6 and PMS2, which are associated with LS when an alteration is present. If a person is born with an alteration in one of these genes they will have an increased chance of developing associated cancers.

Inheritance

Our genes exist in pairs, and we inherit one of each pair from our mother and one from our father. In turn, we pass on one copy of each of our genes to our children as does our partner, so the baby inherits two copies of the gene. LS is inherited in an autosomal dominant pattern. If there is a genetic alteration in the family, those who have been affected with LS-associated cancers are likely to have inherited this alteration. The diagram below shows the chances of passing on the genetic alteration to future

generations. Inheritance is a random process, and the chances with each pregnancy remain at 50%.



Genetic Testing and Possible results

Genetic testing for Lynch syndrome involves having a blood test. DNA is then extracted from the blood to look for alterations in the LS genes. Initial genetic testing can take several months to complete. Possible results include:

1. <u>An alteration is identified</u>
   This result will effectively diagnose you with inherited Lynch Syndrome and is likely to explain your personal history of cancer. You will then be referred to Clinical Genetics to discuss your screening and management options. You will be offered an appointment within a few weeks. Your close relatives (parents, siblings and/or children) will also be eligible for a referral to Clinical Genetics to discuss testing options.
2. <u>No alteration identified</u>
   In this instance, we cannot completely exclude the possibility of a genetic predisposition to cancer in the family. It may be that we have been unable to identify an alteration using current technology or that there may be an alteration in a gene we do not yet test for. You will need to have a discussion with your specialist as to whether a referral to Clinical Genetics is indicated. Your specialist may ask questions about your family history to support their assessment. If you are referred to Clinical Genetics you will be offered a routine appointment.
3. <u>Variant of unknown significance (VUS)</u>
   We may identify an alteration in a gene that is difficult to interpret, and we may be unsure whether it is the cause of your diagnosis. We all have alterations in our genes which contribute to our uniqueness. You will be referred to Clinical Genetics and offered a routine appointment.

Option for DNA storage

We appreciate that now may not be the right time for you to consider genetic testing. We can organise for a sample of your DNA to be stored, for you or your family to look into things in the future.