Molecular subtypes and genetic alterations may determine response to lung cancer therapy

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Cancer therapies targeting specific molecular subtypes of the disease allow physicians to tailor treatment to a patient's individual molecular profile. But scientists are finding that in many types of cancer the molecular subtypes are more varied than previously thought and contain further genetic alterations that can affect a patient's response to therapy.

A UNC-led team of scientists has shown for the first time that lung cancer molecular subtypes correlate with distinct genetic alterations and with patient response to therapy. These findings in pre-clinical models and patient tumor samples build on their previous report of three molecular subtypes of non-small cell lung cancer and refines their molecular analysis of tumors.

Their findings were published in the May 10, 2012 online edition of the Public Library of Science *One*.

Study senior author, Neil Hayes, MD, MPH, associate professor of medicine, says, "It has been known for about a decade of using gene expression arrays that "molecular subtypes" exist. These subtypes have molecular "fingerprints" and frequently have different clinical outcomes. However, the underlying etiologies of the subtypes have not been recognized. Why do tumors form subtypes?

"Our study shows that tumor subtypes have different underlying

alterations of DNA as part of the difference. These differences are further evidence of the importance of subtypes and the way we will use them. For example, the mutations are different which may imply much more ability to target than previously recognized. Also, we are starting to get a suggestion that these subtypes may reflect different cells of origin that rely on different cancer pathways. This is further unlocking the diversity of this complex disease." Hayes is a member of UNC Lineberger Comprehensive Cancer Center.

The team first defined and reported in 2006 on three lung cancer molecular subtypes, named according to their genetic pattern – bronchoid, squamoid and magnoid.

In this *PLoS One* paper they sought to determine if distinct genetic mutations co-occur with each specific molecular subtypes. They found that specific genetic mutations were associated with each subtype and that these mutations may have independent predictive value for therapeutic response.

Provided by University of North Carolina School of Medicine

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