

無創性唐氏綜合症產前檢查研究

屢獲國際傳媒稱許

Noninvasive Prenatal Testing for Down's Syndrome Repeatedly Recognized by World Media

醫學院李嘉誠醫學講座教授及化學病理學講座教授盧煜明教授率領的研究小組，於1997年首度發現母體血漿帶有胎兒的脫氧核糖核酸 (DNA)，其後進而以驗血來檢測唐氏綜合症，開創了無創性產前檢查的新里程。是項研究最近分別獲國際雜誌《時代》周刊 (電子版)、新聞網站ABC News.com和Foxnews.com列為2008年十大重要醫學新聞 / 突破，彰顯中大的研究實力及創新性。

從理論到應用

研究獲此青睞，盧煜明教授深感鼓舞。他說：「經過十一年的研究，終於由基礎的科學發現，進展至臨床測試階段，希望可以造福世界各地數以百萬計的孕婦。香港的生物技術能具有全球的影響力，也令人興奮不已。」盧教授透露中大已授權予一家美國的生物科技公司Sequenom，以其研究為基礎製成試劑，並將於今年6月面世。

盧教授回想，最初因好奇心而探討胎兒的DNA和核糖核酸 (RNA) 能否衝越胎盤這問題，其後真的在母體血漿找到了胎兒的DNA和RNA，於是他再研究這浮游核酸能否反映胎兒從父親遺傳到的基因和基因突變，結果是肯定的。「基於這些研究成果，我們才得以進一步向高難度挑戰，因為檢測唐氏綜合症，必須準確計算出胎兒的21號染色體的數目。」

開創性研究與困難

開創性的研究，自然也遇到全新的困難。盧教授說：「香港的設施不及歐美，因此，每當我們要嘗試採用一種新技術時，就如從零開始，寸進而行。十一年來，這些例子屢見不鮮，如在香港引入實時定量聚合酶連鎖反應、應用基因芯片技術、以質譜分析技術分析DNA、RNA及新一代高流量的DNA序列等。不過，隨着李嘉誠健康科學研究所的成立，以及其先進核心設施的運作，我相信會減少這些研究障礙，有助年輕研究人員全心全意朝着自己的學術理想邁進。」

甚麼是無創性唐氏綜合症產前檢查？ Noninvasive Test for Down's Syndrome

相對正常的胎兒，患唐氏綜合症的胎兒擁有多一條21號染色體 (即是三條)。羊膜穿刺術 (俗稱抽羊水) 是現時唐氏綜合症產前檢查最常用的方法之一，以針管插入羊膜內，取得包圍胎兒的羊水作檢查。惟此法有機會傷及胎兒，導致流產的機率是百分之一。盧教授發現母親血漿帶有胎兒的DNA和RNA，並發展出方法，可量度出血漿內從21號染色體釋放出的DNA或RNA，只要為母親驗血，即可知道胎兒是否患有唐氏綜合症，且敏感度高達九成。

Down's Syndrome is caused by an abnormal number of chromosome 21 (i.e. three in a Down's foetus compared with two in a normal foetus). Currently, testing for Down's Syndrome requires the use of amniocentesis which entails the insertion of a needle into the uterus to take a sample of the amniotic fluid surrounding the foetus. The procedure is invasive and the rate of miscarriage is 1%. Having discovered the presence of cell-free foetal DNA and RNA in the blood plasma of pregnant women, Prof. Lo developed methods for accurately measuring the number of DNA and RNA molecules derived from chromosome 21, leading to a prenatal blood test that, even in the first generation of the test, has an accuracy of over 90%.

Prof. Dennis Y.M. Lo and Team

Blood Test for Down's Syndrome

TOP 10

Medical Breakthroughs (2008), Time

Medical Stories of 2008, ABC News.com

Health Stories and Medical Breakthroughs of 2008, Foxnews.com



盧煜明教授 (後排中) 及其年少有為的研究團隊
Prof. Dennis Y.M. Lo (centre, back row) with his team of young researchers

盧教授正期待新檢查法的臨床應用，「以驗血來檢查唐氏綜合症，不會造成創傷，可以避免傳統檢查百分之一的流產機會，不管是對減輕孕婦的心理壓力或對胎兒的安全都是一個進步。」

In 1997, Prof. Dennis Y.M. Lo, Li Ka Shing Professor of Medicine and Professor of Chemical Pathology, and his research team discovered for the first time in the world the presence of cell-free foetal DNA in the blood plasma of pregnant women. This discovery has recently led to the noninvasive prenatal testing for Down's Syndrome and was listed as one of the top 10 medical stories/breakthroughs of 2008 independently by three international media, namely, Time magazine (electronic version), ABC News.com, and Foxnews.com.

From Theory to Application

Prof. Lo said, 'I am glad to see that after 11 years of research in this area, the work has moved from a basic scientific discovery to a diagnostic test that can potentially benefit millions of pregnant women worldwide. It is also good to see that biotechnologies developed in Hong Kong can make a global impact.' The revolutionary test has been licensed to Sequenom, a US biotechnology company, and a new line of products based on Prof. Lo's technology has been created. The Down's Syndrome test will be launched in June 2009.

Prof. Lo began his research by examining if the placental barrier between the mother and foetus could be breached by DNA and RNA molecules. The result indicated that the foetus could release its DNA and RNA into the mother's circulation, so he initially focused on genes or mutations

passed on to the foetus by the father and which were distinguishable from those of the mother. 'Following the achievement of these initial objectives, we then moved on to the more challenging problem of Down's Syndrome detection. It is more challenging because in Down's Syndrome, we are counting the number of foetal chromosome 21, and this requires much more precise analytical methods.'

Revolutionary Research vs Revolutionary Difficulties

Prof. Lo's revolutionary research brought new challenges. He recalled, 'One difficulty concerns the a lack of core research facilities in Hong Kong compared with the US and Europe. Whenever we tried to use a new technology, we had to establish it from ground up. During the course of the last 11 years, we encountered a number of such scenarios, e.g., the introduction of real-time PCR to Hong Kong, the use of Affymetrix microarray technology, mass spectrometry for DNA/RNA analysis and next-generation DNA sequencing. Now, with the establishment of core facilities at the new Li Ka Shing Institute of Health Sciences, I hope that such barriers to research will be lowered, thus helping our younger researchers to launch their careers more rapidly.'

With the use of a noninvasive blood test for Down's Syndrome, Prof. Lo expected that the 1% spontaneous abortion resulting from invasive testing could be avoided. 'I think such developments would make prenatal testing safer for the foetus and less traumatic, both psychologically and physically, for the mother,' he observed. 📷