# 全港首宗基因療法 一針提高 SMA病童存活率

## The first gene therapy improves survival rates of young SMA patients



隨著醫學科技進步，基因療法將不可能變可能，讓人束手無策的疾病亦見轉機。以往脊髓肌肉萎縮症（SMA）病人須終身接受治療，包括每三至四個月到醫院進行脊髓注射，或每日服用口服藥物。醫管局最新引入全港首個基因療法，只要透過靜脈注射用藥一次，便能提高患者存活率。

「幾個月就要到醫院打針，對孩子來說是創傷的記憶。基因療法一針見效，療程一小時，可以免除長期治療的不便，給患者及整個家庭帶來新希望。」醫管局總藥劑師**李成章**博士解釋，SMA患者因基因缺陷，無法產生足夠功能的蛋白質，影響活動能力；「阿哌奧諾基」基因療法將帶有基因的無害病毒載體注入病人體內，讓基因發揮基本功能，彌補先天不足，患者手腳可以正常活動，亦能擺脫永久使用呼吸機。持續的臨床數據顯示，療效在注射七年半後仍然存在。

醫管局聯網服務總監**鄧耀鏗**醫生說：「當知道有基因療法可以醫治SMA患者後，醫管局在短時間內與藥廠協議免費提供一劑新藥作臨床治療，脊髓肌肉萎縮症專家小組亦為基因療法擬定臨床用藥指引。團隊其後成功申請新藥納入關愛基金極度昂貴藥物項目資助範圍，讓更多病人受惠。」



（右起）鄧耀鏗醫生及李成章博士表示，將適時引入對其他疾病有成效的基因療法。

(From right) Dr Simon Tang and Dr Benjamin Lee state that gene therapies that are effective for other diseases will be introduced timely.

鄧醫生回想過程中最具挑戰局面，在於團隊要決定哪名病人使用首支新藥。「當時新藥尚待納入關愛基金資助項目，我們就只有一針，全靠脊髓肌肉萎縮症專家小組基於臨床評估選擇病人；慶幸現時已獲批資助，只要符合臨床用藥指引，每名合適患者都可接受基因療法。」

### 逾30人跨專業團隊 萬全準備



引入基因療法的事前準備亦非常講究，香港兒童醫院行政總監**李子良**醫生（圖）分享，該院有超過30人的跨專業團隊曾接受相關培訓，醫院規格亦符合要求，包括藥劑部安排特定生物安全櫃，仔細規劃及訓練如何運送、雪藏和解凍該針劑，並且要確保在無菌環境下進行藥物調配。由於注射後病人有機會出現發燒、嘔吐等副作用，醫護團隊後續細心照顧病童，持續觀察其肝酵素和驗血報告；而物理治療師、職業治療師及言語治療師亦會定期評估其發展進度。

李醫生說：「今次是難得的學習機會，因我們以後會照顧第二、第三個接受基因療法的小朋友，必須從一開始便做好最全面的準備，達至國際標準。眼見孩子在同事的悉心照顧下有好轉，醫護團隊十分鼓舞。」

With the advancement of medical science and technology, gene therapy has made the impossible possible, and diseases that have left people powerless have seen a turnaround. In the past, patients with spinal muscular atrophy (SMA) had to undergo life-long treatment, including spinal injections in hospitals every three to four months or daily oral medication. Now, the Hospital Authority (HA) has introduced gene therapy, significantly improving the survival rate of SMA patients with the one-time intravenous administration of a drug.

"Having to go to the hospital for injections every few months is a traumatic experience for a child. The infusion of the one-time gene therapy takes only an hour. It can eliminate the inconvenience of long-term treatment and bring new hope to the patient and the whole family," explains HA Chief Pharmacist Dr **Benjamin Lee**. Patients with SMA are unable to produce enough functioning proteins because of genetic defects which result in the loss of motor muscle functions. The new gene therapy, Onasemnogene abeparvovec, involves injecting a harmless viral vector carrying the corresponding genes into the patient's body, which allows the genes to perform their basic functions and compensates for congenital deficiencies so that patients can maintain their muscle functions normally and avoid the need to use ventilator. On-going clinical data shows that the effects of the new drug last for up to 7.5 years after it is administered.

HA Cluster Services Director Dr **Simon Tang** says, "once the HA knew that gene therapy could benefit some SMA patients, we negotiated with the pharmaceutical company to provide one dose of the new drug free of charge for clinical treatment. In parallel, the SMA expert panel formulated clinical guidelines for the new drug, and we also successfully applied for the drug to be included in the ultra-expensive drug category of the Community Care Fund (CCF) for subsidising families of SMA patients with financial needs."

The team was facing challenges in selecting the first patient for treatment. "At that time, the new drug had yet to be included in the CCF and we only had one injection. We are grateful to the SMA expert panel for selecting the patient based on clinical evidence," Dr Tang recalls. "Thankfully, the new drug has now been covered by the CCF, so in future any SMA children who meet the clinical guidelines for the new drug will be able to receive it."

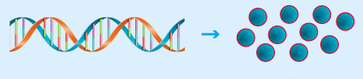
### A team of dedicated experts on standby

Preparations for the gene therapy were also well-planned. A multi-disciplinary team of more than 30 professionals is on standby to provide gene therapy, and the hospital specifications also meet the necessary requirements, says Hospital Chief Executive of Hong Kong Children's Hospital Dr **Lee Tsz-leung** (photo). Preparations include arranging a designated biological safety cabinet, along with the well planning and training by staff of pharmacy department on how to handle, store, and thaw the injectable drug, and ensuring aseptic preparation of the drug infusion. As side effects such as fever and vomiting may occur after the injection, the medical team provided careful post-treatment care, and closely monitored the baby's liver enzymes and blood test results. Physiotherapists, occupational therapists, and speech therapists then regularly assessed the baby's progress.

"This is a valuable learning opportunity as we will be caring for more children receiving gene therapy in the future," says Dr Lee. "We must be fully prepared and meet the international standard from the outset. Our medical team is greatly encouraged by the improvement of conditions of the baby."

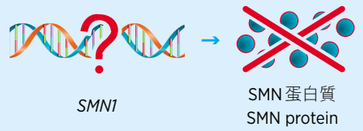
### 圖解 SMA基因療法 About SMA gene therapy

健康 SMN1 基因產生正常功能的 SMN 蛋白質。
A healthy SMN1 gene produces SMN protein.



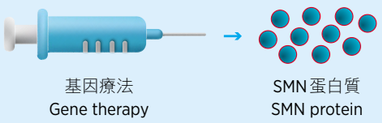

SMA 患者出生時缺少或擁有無法正常運作的 SMN1 基因，導致無法產生足夠正常功能的 SMN 蛋白質，肌肉逐漸無力萎縮。

SMA patients are born without or with a non-functioning SMN1 gene, which results in a failure to produce enough SMN protein to function properly, and leads to muscle weakness and atrophy.




基因療法使用非複製型腺病毒9型（scAAV9）載體，經一次靜脈注射，將正常的 SMN1 基因注入患者體內，從而製造正常功能的 SMN 蛋白質，改善運動功能。

With the use of self-complementary adeno-associated virus (scAAV9), gene therapy is to inject the normal SMN1 gene one time into the patient's body via intravenous injection, thereby producing normal functioning SMN proteins, improving the motor functions.



# 出世手腳無力 醒目寶寶學識「請請」

## Gene therapy helps baby boy defy the odds





寶寶平安長大是每個父母的願望，但有一名男嬰出生兩周已出現手腳無力等病徵，其後確診 SMA 一型，令父母忐忑不安。男嬰之後接受傳統藥物「諾西那生」治療，並在10個月大時成為本港首宗受助於基因療法的個案。眼見男嬰病情有好轉，主診的兒童腦神經科醫生**陳凱珊**（圖）不禁笑逐顏開：「他最近學會了『請請』和握手，在輔助下站起來，還會在電腦前『扮工』，是非常醒目的寶寶！」

陳醫生是香港兒童醫院兒童及青少年科榮譽顧問醫生及香港大學臨床副教授，她說男嬰最初是在一項新生兒篩查中確診 SMA 一型，首兩個月需每隔二至四周進行一次「諾西那生」腰椎穿刺，之後每四個月注射一次。隨後幾個月，男嬰已可自行轉身和坐起來。「當父母知道本港引入基因療法，男嬰將有機會接受治療，他們都很激動，因為這是一次性治療。」她解釋，基因療法適用於六個月或以下尚未有病徵或病徵輕微的嬰兒，七至12個月大則會額外評估，肝功能異常或對病毒載體有抗體的患者不能接受基因療法。

SMA 是一種嚴重疾病，未有治療方法問世之前，陳醫生有不少 SMA 病人要長期使用呼吸機、胃造口餵食、坐輪椅，並有嚴重脊柱側彎等。縱使面對種種挑戰，他們依然展示出才華洋溢和明亮一面，在學業和課外活動上表現傑出，尤其是藝術。陳醫生強調，父母堅持為孩子帶來最佳不受限制的生活十分重要，激勵醫護人員為病人提供最好支援。

隨著公立醫院提供 SMA 新生兒篩查，有助及早診斷病症，在嬰兒未出現病徵或病徵輕微時提供治療，「作為醫護，我們必須爭分奪秒，確保 SMA 寶寶盡快接受變革性治療。我們與家屬都希望寶寶能健康成長，正常發展。」

Parents naturally hope for their children to grow up healthy. However, the parents of a baby boy faced immense anxiety when they discovered their son had muscle weakness just two weeks after birth and was diagnosed with spinal muscular atrophy (SMA) type 1. Initially, this baby boy received Nusinersen for his SMA. At 10 months old, he became the first child in Hong Kong to undergo gene therapy. Dr **Sophelia Chan** (photo), the attending Paediatric Neurologist, is delighted with his progress, and says, “he recently learned to shake hands, stand up with assistance, and sit alone playing with the computer keyboard. He is truly an adorable baby.”

Dr Chan, Honorary Consultant of the Department of Paediatrics and Adolescent Medicine at Hong Kong Children’s Hospital (HKCH) and Clinical Associate Professor at the University of Hong Kong, explains that the baby boy was initially diagnosed with SMA type 1 through newborn screening. For the first two months, he received Nusinersen via lumbar puncture every two to four weeks, followed by similar intrathecal injections every four months. In the months that followed, the baby boy could roll over and sit on his own. Dr Chan recalls, “when the family learned that gene therapy was available in Hong Kong and their son had the opportunity to receive this therapy, they were excited as it is a one-time treatment.” Gene therapy is typically suitable for infants who are six months or younger and display either no symptoms or mild symptoms. Infants between seven to 12 months old require separate evaluations, and those with liver dysfunction or antibodies against the viral vector cannot receive this therapy.

SMA is a severe condition. Before the availability of SMA treatment, many of Dr Chan’s patients required long-term ventilator support, gastrostomy feeding, on wheelchair and experienced severe spinal curvature. Despite these challenges, her patients often display remarkable talent and brightness, excelling in academic and recreational activities, particularly in art. Dr Chan emphasises the importance of parental determination to provide the best-unlimited life to their children, which inspires healthcare professionals to offer the best support to their kids.

With universal SMA newborn screening in public hospitals, early diagnosis is now possible, allowing prompt initiation of treatment even before symptoms appear or while they are still mild. Dr Chan passionately emphasises, “as healthcare professionals, we must race against time to ensure our SMA babies receive transformative treatment as soon as possible. United with families, we hope all the affected children can grow up healthy and even develop normally with treatment.”



父母心聲
Parents’ sharing

男嬰父母感謝陳凱珊醫生（右）及瑪麗醫院、香港兒童醫院和東區尤德夫人那打素醫院醫護團隊等的悉心照料。

The boy’s parents express their gratitude to Dr Sophelia Chan (right) and the medical teams at Queen Mary Hospital, HKCH and Pamela Youde Nethersole Eastern Hospital for their attentive care.

### 脊髓肌肉萎縮症知多點 Know more about SMA

SMA 是一種遺傳性神經肌肉疾病，特徵是脊髓和腦幹下方運動神經元持續衰退，導致階段性肌肉無力和萎縮，失去行動能力，呼吸、吞嚥和口腔進食逐漸變得困難。在本港新生兒篩查中，估計每年將檢測出約一至五名 SMA 患者適合最早使用基因療法，或其他可改善病情進展的治療。

SMA is a genetic neuromuscular disease characterised by persistent degeneration of motor neurons in the spinal cord and lower brainstem, resulting in progressive muscle weakness and atrophy, loss of mobility, and gradual difficulty in breathing, swallowing, and feeding. It is estimated that about one to five SMA patients will be detected each year in Hong Kong during newborn screening and will be suitable for the earliest treatment with gene therapy or other disease-modifying treatment.

| 類型 Type | 發病年齡 Age of onset | 症狀 Symptoms | 存活率 Survival rate | 佔 SMA 比例 Percentage in SMA |
|---|---|---|---|---|
| 一型 Type 1 | 6個月前 <6 months | 不能坐穩，常見呼吸問題及吞嚥困難，症狀隨時間惡化 Unable to sit. Breathing problems and swallowing difficulties are common, with deterioration over time | 多數在兩歲前死亡 Average lifespan of about 2 years of age | 60% |
| 二型 Type 2 | 7-18個月 7-18 months | 可以坐穩，但無法行走。常見失去坐立能力並出現呼吸問題、吞嚥困難及脊柱側彎，症狀隨時間惡化 Able to sit but unable to walk. Loss of sitting ability, having breathing problems, swallowing difficulties, and scoliosis are common, with deterioration over time | 多數能夠活到早期成年 Many infants live to early adulthood | 25-30% |
| 三型 Type 3 | ≥18個月 ≥18 months | 可自行行走，常見失去行走能力和出現脊柱側彎，症狀隨時間惡化 Can walk alone. Loss of walking ability and development of scoliosis are common, with deterioration over time | 正常預期壽命 Normal life expectancy | 10-15% |
| 四型 Type 4 | ≥21歲 ≥21 years old | 可自行行走，慢慢變得四肢無力 Can walk alone, slowly progressive limb-girdle weakness | | 1% |