医薬品
医薬部外品　研究報告　調査報告書
化粧品

識別番号・報告回数		回	報告日 年　月　日	第一報入手日 2008 年 6 月 4 日	新医薬品等の区分 該当なし	総合機構処理欄
一般的名称			研究報告の公表状況	New arenavirus discovered in Bolivia Lancet Infect Dis 2008; 8: 355	公表国 米国	
販売名（企業名）						

研究報告の概要

ボリビア，ペルー及び米国疾病予防管理センター（CDC）の国際チーム（アトランタ，ジョージア州，米国）はボリビアの出血熱の死亡症例において新型のアレナウイルスを発見した。完全ゲノム解析でアレナウイルス属の新型ウイルスであることが認められ，アンデス山脈の山麓にちなんで Chapare virus と名付けられた。当該ウイルスは，系統発生学的には南米で出血熱を自然発生させる他のアレナウイルス，特にサビアウイルスに近いウイルスであった。疾病管理予防センター研究調査員の Stuart Nichol は，「アレナウイルスに関連した出血熱は，アルゼンチン（フニンウイルス），ボリビア（マチュポウイルス及び，現在は Chapare virus），ベネズエラ（グアナリトウイルス）及びブラジル（サビアウイルス）で報告されている。年間の症例数は地域を合わせて数十件から数百件前後まで大きなばらつきがある」とし，また，「Chapere virus がげっ歯類を宿主として長期間存在してきた可能性は非常に高いが，人類への波及はおそらくまれであったと思われる」とも述べている。ハーバード大学医学部（ボストン，マサチューセッツ州，米国）の Michael Farzan 氏は，「南米の野生のげっ歯類において複製するウイルスが人類への感染能を獲得し，重篤な疾患を引き起こすことは容易に起こり得る。これらのげっ歯類の生息環境は様々な形で人類によって破壊されてきていることからも，この点が心配される」と述べている。ウガンダでは，赤オナガザルにおける血清学的検査で新型ポックスウイルスの可能性があるウイルスが発見された。イリノイ大学（Urbana，イリノイ州，米国）主席研究員の Tony Goldberg 氏はこのウイルスは既知のオルソポックスウイルスに類似しているが全く同じものではないとし，さらに「近い将来にこの新型のウイルスが人類に感染する可能性はおそらく低く，また当該研究分野においてポックスウイルスがヒトに感染したエビデンスはない。我々の試験が主に示唆することは，環境において新型であり，また実体の明らかでないポックスウイルスが存在するということである」と述べた。しかしながら，Goldberg は，ポックスウイルスは種のバリアを乗り越えることで悪評が高いことも指摘している。双方の新型ウイルスで懸念されるのは，新たに出現した感染が過去 50 年で約 4 倍に増加しており，野生動物の疾患がこうした疾患の大半を占めているということである。

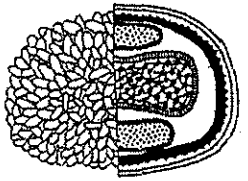
使用上の注意記載状況・その他参考事項等

BYL-2008-0336

PLoS Pathog 2008; 4: e1000047; DOI:10.1371/journal.

Emerg Infect Dis 2008; 14: http://www.cdc.gov/eid/content/14/5/801.htm

Arenavirus



報告企業の意見	今後の対応
2 種類の新規ウイルス病原体はどちらもエンベロープウイルスであり，血漿分画製剤の製造工程におけるウイルス除去・不活化工程により除去・不活化されるウイルスである。また，本報告では新たに出現した感染が過去 50 年で約 4 倍に増加していることを強調している。血漿分画製剤の製造工程におけるウイルス除去・不活化工程は，新たに出現するエンベロープウイルスに対しては効果的であるが，非エンベロープウイルスに対しては未だ完全であるとは考えられない。	今後も，新規ウイルス病原体の出現に関する情報収集に努める。

Highlights from the 18th ECCMID

First European Infection Day

The launch of the first European Day of Fighting Infection took place at the 18th annual European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in Barcelona, Spain (April 19–23). "We need to make people more aware of infections, and to highlight to the general public in particular that everyone can play a part—for example, in the correct use of antibiotics", Giuseppe Cornaglia (University of Verona, Italy) told *TLID*. "The day will also serve to reinforce collaborations between all players in the field of infectious diseases in Europe and to improve knowledge", he added. The day has been created to mark the 25th anniversary of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). "An important aim for us now is to work towards fostering greater collaboration between eastern and western Europe, through professional exchange and improving our support to young scientists."

ECCMID research highlights

A key focus of the meeting was around antibiotic resistance in Europe and how best to ensure more rational use of antibiotics by clinicians. In a press conference, Fernando Baquero (Hospital Ramón y Cajal, Madrid, Spain) said clinicians are particularly concerned about resistance to antibiotics commonly used in children. He said: "Innovative antibiotics are not being developed, and industrial research facilities on antimicrobial agents are increasingly being shut down...we therefore cannot use all the antibiotics commonly available for use in adults for the treatment of children".

Sore throats are common in children, yet only 15–30% of them are caused by pathogenic bacteria, most frequently group A streptococci. In an expert session, Paul Little (University of Southampton, UK) warned clinicians against prescribing antibiotics immediately. "There are several alternatives: if rapid streptococcal tests are available it takes just 5 min to exclude or confirm infection. If a rapid test is not available, it's safe to wait 3 days before using antibiotics", he said. Antibiotic therapy should be started after 3–4 days if necessary, "in the meantime you can give anti-inflammatory drugs to control the symptoms".

E Tacconelli and colleagues (Catholic University, Rome, Italy) did a 1-year cohort study to analyse the risk factors for infections by antibiotic-resistant bacteria in hospital admissions. Infections caused by antibiotic-resistant bacteria were diagnosed in 398 patients (seven cases per 1000 admissions). They report an increased risk associated with colonisation in patients aged >60 years with urinary catheters and clinical signs of bacterial infections at admission and in patients previously treated with antibiotics, and conclude that greater recognition of these risk factors may influence the selection of empirical treatment.

Sally Hargreaves

The printed journal includes an image merely for illustration

For more on ESCMID see http://www.escmid.org

New arenavirus discovered in Bolivia

An international team from Bolivia, Peru, and the US Centers for Disease Control and Prevention (CDC, Atlanta, GA, USA) has discovered a new arenavirus in a fatal case of haemorrhagic fever in Bolivia. Complete genome analysis revealed a distinct member of the arenavirus family; named Chapare virus, after a river in the foothills of the Andes. The virus is phylogenetically related to other arenaviruses that naturally cause haemorrhagic fever in South America, particularly Sabia virus.

Study investigator Stuart Nichol (CDC) said that "arenavirus-associated haemorrhagic fever has been described in Argentina (Junin virus), Bolivia (Machupo and now Chapare virus), Venezuela (Guanarito virus), and Brazil (Sabia virus). The number of cases per year varies substantially, from around a few hundred cases down to double digits for the whole region". Nichol added: "It is highly likely that Chapere virus has been present in a rodent reservoir for a long time, although spill-over to human beings is probably infrequent". Michael Farzan (Harvard Medical School, Boston, MA, USA) said: "The discovery underscores the ease with which viruses replicating in South American wild rodents can acquire the ability to infect human beings and cause serious disease. This is especially a concern, since the natural habitats of these rodents are being disrupted in a variety of ways".

A possible new poxvirus has been discovered following serological tests in red colobus monkeys in Uganda. Lead investigator Tony Goldberg (University of Illinois, Urbana, IL, USA) said that the virus is similar, but not identical, to known orthopoxviruses, which includes smallpox virus.

Goldberg added: "The likelihood of the new virus infecting human beings in the near future is probably low; there was no evidence of human poxvirus infection in the study area. One of the main implications of our study is that there are new, as yet unidentified poxviruses in the environment". Nevertheless, Goldberg pointed out that poxviruses are notorious for crossing species barriers.

The concern with both new viruses is that emerging infections have roughly quadrupled over the past 50 years, and that wildlife zoonoses account for the majority of such diseases.

Cathel Kerr

For more on Chapare virus see *PLoS Pathog* 2008; 4: e1000047; DOI:10.1371/journal.ppat.1000047

For more on the novel poxvirus in colobus monkeys in Uganda see *Emerg Infect Dis* 2008; 14: http://www.cdc.gov/eid/content/14/5/801.htm

For more on emerging infectious diseases and wildlife zoonoses see Newsdesk *Lancet Infect Dis* 2008; 8: 218–19

医薬品　研究報告　調査報告書

識別番号・報告回数			報告日	第一報入手日 2008年9月16日	新医薬品等の区分 該当なし	総合機構処理欄
一般的名称	別紙のとおり		研究報告の公表状況	Proc Natl Acad Sci U S A. 2008;105:14124-14129	公表国 米国	
販売名（企業名）	別紙のとおり					

研究報告の概要

問題点：齧歯類の重症疾患の原因ウイルスとされていた cardiovirus がヒトにおいても存在することが遺伝子学的手法により確認された。

齧歯類の重症疾患の原因となる picornavirus 科に属する cardiovirus は、その罹患率、多様性、ヒトでの症状等についてはあまり知られていない。発熱のある乳児の便検体から 1981 年に培養された Saffold virus は、cardiovirus に分類されている。今回、患者検体から直接ヒト cardiovirus をクローニングしたことについて報告する。これはインフルエンザ様の症状を示した子供の呼吸分泌物から pan-viral microarray 法を用いて発見した最初の報告である。ほぼ全長のウイルスゲノム(7961 bp)の系統樹解析で、ウイルスは cardiovirus のサブグループである Theiler's murine encephalomyelitis virus(TMEV)に属し、Saffold virus と最も密接に関係があった。719 の呼吸器サンプル（急性呼吸器症状を示した患者からは 637 検体(89%)）と神経系疾患患者（無菌性髄膜炎、脳炎及び多発性硬化症）からの髄液検体 400 の RT-PCR によるスクリーニングでは、cardiovirus 感染の痕跡は認められなかった。しかし、胃腸炎患者 498 人の排泄物 751 検体のスクリーニングの結果、6 検体より cardiovirus（1.2%）が検出された。これら Saffold virus を含む 8 つのヒト cardiovirus は、系統樹解析によりすべて同じところにクラスターされたが、VP1 遺伝子にかなりの多様性が認められた(アミノ酸の相同性は 66.9%–100%)。これらの結果は、これまでほとんど確認されていなかったが、現在は主に消化管において確認され、無症候で排出され、そして腸内外の疾患に関連している可能性がある新しいヒト TMEV 様の cardiovirus の多様な集団が存在することを示唆している。

報告企業の意見	今後の対応
別紙のとおり	今後とも関連情報の収集に努め、本剤の安全性の確保を図っていきたい。

使用上の注意記載状況・その他参考事項等

記載なし

MedDRA/J ver.11.1

別紙

一般的名称	①人血清アルブミン、②人血清アルブミン、③人血清アルブミン*、④人免役グロブリン、⑤乾燥ペプシン処理人免疫グロブリン、⑥乾燥スルホ化人免疫グロブリン、⑦乾燥スルホ化人免疫グロブリン*、⑧乾燥濃縮人活性化プロテインC、⑨乾燥濃縮人血液凝固第Ⅷ因子、⑩乾燥濃縮人血液凝固第Ⅸ因子、⑪乾燥抗破傷風人免疫グロブリン、⑫抗 HBs 人免疫グロブリン、⑬トロンビン、⑭フィブリノゲン加第ⅩⅢ因子、⑮乾燥濃縮人アンチトロンビンⅢ、⑯ヒスタミン加人免疫グロブリン製剤、⑰人血清アルブミン*、⑱人血清アルブミン*、⑲乾燥ペプシン処理人免役グロブリン*、⑳乾燥人血液凝固第Ⅸ因子複合体*、㉑乾燥濃縮人アンチトロンビンⅢ
販売名(企業名)	①献血アルブミン 20 “化血研”、②献血アルブミン 25 “化血研”、③人血清アルブミン “化血研” *、④ “化血研” ガンマーグロブリン、⑤献血静注グロブリン “化血研”、⑥献血ベニロンー I 、⑦ベニロン*、⑧注射用アナクトC2,500 単位、⑨コンファクトF、⑩ノバクトM、⑪テタノセーラ、⑫ヘパトセーラ、⑬トロンビン “化血研”、⑭ボルヒール、⑮アンスロビンP、⑯ヒスタグロビン、⑰アルブミン 20%化血研*、⑱アルブミン 5%化血研*、⑲静注グロブリン*、⑳ノバクトF*、㉑アンスロビンP 1500 注射用
報告企業の意見	cardiovirus は、picornavirus 科に分類される属名の一つである。cardiovirus 属のウイルスはエンベロープを持たず、直径約 30nm で正 20 面体のカプシッドを持ち、核酸は一本のプラス鎖 RNA である。cardiovirus 属には次の 2 つのサブグループがある；脳心筋炎ウイルス (encephalomyocarditis virus ; EMCV)、タイラーのマウス脳脊髄炎ウイルス (Theiler's murine encephalomyelitis virus ; TMEV)。これらのウイルスは、げっ歯類に感染し消化器官で増殖した後、糞便経口ルートで伝播する。ウイルスが腸管感染しても大抵は軽度か無症状であるが、腸管外に拡がると全身性の疾患を惹き起こす。EMCV 系統のウイルスは脳炎及び心筋炎を惹き起こし、TMEV 系統のウイルスは中枢神経系感染に関連している。ヒトから分離されたとされる cardiovirus 属のウイルスも報告されているが、ヒトから直接クローニングされたことはなく、その罹患率、多様性、ヒトでの症状等についてはあまり知られていない。 本剤の製造工程には、冷エタノール分画工程、ウイルス除去膜ろ過工程あるいは加熱工程等の原理の異なるウイルス除去及び不活化工程が存在しているので、ウイルスクリアランスが期待される。各製造工程のウイルス除去・不活化効果は、「血漿分画製剤のウイルスに対する安全性確保に関するガイドライン (医薬発第 1047 号、平成 11 年 8 月 30 日)」に従い、ウシウイルス性下痢ウイルス (BVDV)、仮性狂犬病ウイルス (PRV)、ブタパルボウイルス (PPV)、A 型肝炎ウイルス (HAV) または脳心筋炎ウイルス (EMCV) をモデルウイルスとして、ウイルスプロセスバリデーションを実施し、評価を行っている。今回報告した cardiovirus 属には、モデルウイルスとして使用している EMCV そのものが属しており、上記バリデーションの結果から、本剤の製造工程が EMCV の除去・不活化効果を有することを確認している。また、これまでに本剤による cardiovirus 感染の報告例は無い。 以上の点から、本剤は cardiovirus に対する安全性を確保していると考える。

*現在製造を行っていない

Identification of cardioviruses related to Theiler's murine encephalomyelitis virus in human infections

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Cardioviruses comprise a genus of picornaviruses that cause severe illnesses in rodents, but little is known about the prevalence, diversity, or spectrum of disease of such agents among humans. A single cardiovirus isolate, Saffold virus, was cultured in 1981 in stool from an infant with fever. Here, we describe the identification of a group of human cardioviruses that have been cloned directly from patient specimens, the first of which was detected using a pan-viral microarray in respiratory secretions from a child with influenza-like illness. Phylogenetic analysis of the nearly complete viral genome (7961 bp) revealed that this virus belongs to the Theiler's murine encephalomyelitis virus (TMEV) subgroup of cardioviruses and is most closely related to Saffold virus. Subsequent screening by RT-PCR of 719 additional respiratory specimens [637 (89%) from patients with acute respiratory illness] and 400 cerebrospinal fluid specimens from patients with neurological disease (aseptic meningitis, encephalitis, and multiple sclerosis) revealed no evidence of cardiovirus infection. However, screening of 751 stool specimens from 498 individuals in a gastroenteritis cohort resulted in the detection of 6 additional cardioviruses (1.2%). Although all 8 human cardioviruses (including Saffold virus) clustered together by phylogenetic analysis, significant sequence diversity was observed in the VP1 gene (66.9%–100% pairwise amino acid identities). These findings suggest that there exists a diverse group of novel human Theiler's murine encephalomyelitis virus-like cardioviruses that hitherto have gone largely undetected, are found primarily in the gastrointestinal tract, can be shed asymptomatically, and have potential links to enteric and extraintestinal disease.

DNA microarrays | gastroenteritis | influenza-like illness | picornavirus | virus discovery

Picornaviruses are positive single-stranded RNA viruses that cause a variety of important disease states in humans and animals. Several genera of picornaviruses are recognized, based on genomic sequence and virus biology. The *Cardiovirus* genus of the family Picornaviridae consists of two subgroups: Theiler's murine encephalomyelitis virus (TMEV) and related viruses (Theiler-like virus NGS910 of rats, Vilyuisk virus) (1–3), and encephalomyocarditis virus (EMCV) and related viruses (EMCV, Mengovirus, Columbia SK virus, Maus–Elberfeld virus) (4). All these viruses infect rodents, replicate in the gastrointestinal (GI) tract and are transmitted by the fecal-oral route. Although enteric infection by these viruses is often mild or asymptomatic, extraintestinal spread of these viruses can occur and can lead to systemic disease (1). As their name implies, the EMCV-like agents cause encephalitis and myocarditis, whereas the TMEV family is linked to CNS infection. In experimental settings, intracerebral inoculation of mice with TMEV can produce acute encephalomyelitis and/or a chronic demyelinating disease resembling human multiple sclerosis (MS), depending upon the strain of TMEV used (5). Oral inoculation with TMEV may also result in encephalomyelitis, especially when large inocula are delivered to neonatal mice (6).

Whether authentic human cardioviruses exist has long been debated. The first candidate human cardiovirus was Vilyuisk virus, which was linked to Vilyuisk encephalitis, an unusual neurodegenerative disease found among the Yakuts people of Siberia in the 1950s and still endemic to the region (7, 8). The Vilyuisk virus was initially isolated from the cerebrospinal fluid (CSF) of an affected patient and underwent 41 serial passages in mice before sequencing and characterization as a TMEV-like picornavirus (3, 9). Given its sequence similarity to TMEV and its extensive passage history in mice, questions have arisen as to whether the virus may in fact be of murine origin. In 1981, another TMEV-related cardiovirus was cultured from the stool of an infant who presented with a febrile illness (10). Although early passages appeared to show that the virus was transmissible, long-term continuous propagation of the isolate has been problematic. The nearly complete genomic sequence of this isolate (provisionally called Saffold virus) was recovered from frozen stocks by cloning in 2007 and was found to be much more divergent from TMEV than Vilyuisk virus (10). However, neither Vilyuisk nor Saffold virus was cloned directly from primary clinical specimens, and the diversity, prevalence, and potential clinical manifestations of human cardiovirus infection have remained largely unexplored.

We have previously developed a pan-viral DNA microarray (Virochip; University of California, San Francisco) designed to detect known and novel viruses in clinical specimens on the basis of homology to conserved regions of known viral sequences (11). The current study uses microarrays from the third and fourth generations of this platform (Viro3, Viro4). The Viro3 platform has 19,841 viral oligonucleotides derived from all publicly available viral sequence as of June 2004 (12, 13). The Viro4 platform is a streamlined update of the Viro3 platform consisting of 14,740 viral oligonucleotides derived from all publicly available viral sequence as of June 2006. The Virochip has been used to detect novel pathogens such as the severe acute respiratory syndrome coronavirus (14) and XMRV, a retrovirus identified in prostate tissue of men with germ-line mutations in RNase L (15). The platform has also been successfully used to detect

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The authors declare no conflict of interest.

Freely available online through the PNAS open access option.

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known and divergent viruses in acute respiratory tract infections in several recently published studies (12, 13, 16, 17).

In this study, we used the Virochip to screen respiratory secretions from patients with influenza-like illness who lacked a diagnosis despite extensive microbiological testing. In one such patient, we detected and fully sequenced a cardiovirus in the Saffold group. Related cardioviruses were subsequently found in stool specimens from an additional six individuals collected as part of a study examining household transmission of gastroenteritis (18). We report here the existence and overall phylogeny of a diverse group of human cardioviruses and discuss their potential association with human disease.

Results

Detection of a Cardiovirus in a Patient with Influenza-Like Illness. A total of 460 respiratory secretions from patients meeting a case definition of influenza-like illness were screened for respiratory viruses by culture. In 108 culture-negative specimens selected from elderly and pediatric patients, 16 specimens remained negative after subsequent RT-PCR testing for respiratory syncytial virus (RSV), influenza A/B (Flu A/B), rhinovirus (RV), and enterovirus (EV). These 16 specimens were assayed for the presence of viruses using the Virochip (Viro3), with microarray analysis carried out using E-Predict and ranked z score analysis, as previously described (12, 19).

Four of the 16 specimens yielded a positive microarray hybridization signature suggestive of a virus. Two of the signatures corresponded to metapneumovirus, one signature corresponded to adenovirus, and one signature indicated the presence of a cardiovirus related to TMEV. From the microarray containing the cardiovirus signature, the highest intensity oligonucleotides mapped to the 5′-untranslated region (5′-UTR) and 2C gene of the TMEV genome, the most conserved regions among cardioviruses and picornaviruses in general (Fig. 1*A*, "ARRAY"). To recover viral sequence, we designed primers based on the highest intensity array features and alignment of well conserved sequences from four cardioviruses (TMEV-DA, TMEV-GDVII, Theiler-like NGS910 virus, and EMCV). One set of primers successfully amplified a 224-bp fragment from the viral 5′-UTR. The fragment shared 90% nucleotide identity with the 5′-UTR region of Theiler-like NGS910 virus. This finding established that the virus in question was indeed a cardiovirus and a relative of the TMEV group of viruses. We designated this initial cardiovirus strain UC1.

Complete Genome Sequencing and Analysis of UC1. To clone and sequence the remainder of the UC1 genome, additional short fragments were first obtained from conserved regions in the 2C (helicase) and 3D (polymerase) genes by use of consensus PCR primers derived from alignment of the four cardioviruses mentioned previously. Long-range RT-PCR using specific primers was then used to bridge the gaps. This resulted in PCR amplification of two long overlapping fragments (≈5.3 and 3.7 kB in size) jointly spanning nearly the entire length of the virus genome (Fig. 1*A*, "RT-PCR"). Cloned ends of the genome were recovered and sequenced using a RACE amplification protocol (20, 21).

The nearly complete sequence of UC1 is 7961 nt in length and forms a distinct branch in the *Cardiovirus* genus with Saffold virus (Fig. 1*B*). The overall nucleotide identity to Saffold virus is >90% in the 5′-UTR and the region coding for the nonstructural proteins but only 70% in the region coding for the capsid proteins (Fig. 1*A*, "Saffold"). There is much less overall nucleotide sequence identity to other members of the TMEV subgroup (70–80%) and EMCV (50–55%). A poly(C) tract that has been reported in EMCV but not in TMEV strains is not present in the 5′-UTR of UC1. Similar to other cardioviruses, the ORF of UC1 is predicted to code for a single 2296-amino acid polyprotein that is subsequently cleaved into the L protein, the

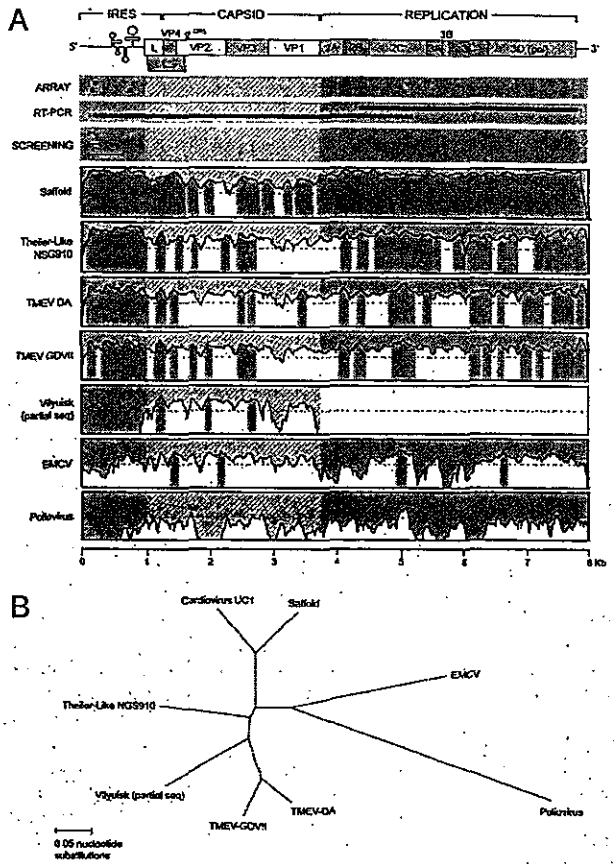

Fig. 1. Genome sequence of UC1. (*A*) Genome sequence similarity plots compare UC1 with Saffold virus, Theiler-Like NGS910 virus, TMEV-DA, TMEV-GDVII, Vilyuisk virus (partial sequence only), EMCV, and poliovirus. The y axis scale for each plot represents percentage of nucleotide identities from 0% to 100%. Regions of the genome with percentage of nucleotide identities of >70% are highlighted in pink. The Virochip oligonucleotides used to detect UC1 ("ARRAY"), the fragments generated by long-range RT-PCR and used to sequence most of the virus ("RT-PCR"), and the cardiovirus primers and resulting PCR fragments used for screening of stool, CSF, and respiratory secretions ("SCREENING") are also shown mapped onto the UC1 genome. The sequences of these primers are provided in Table S1. (*B*) Radial tree depicts the phylogenetic relationships between the genomes of UC1 and the seven aforementioned cardioviruses.

capsid proteins (VP1, VP2, VP3, and VP4), and nonstructural proteins involved in viral replication (2A, 2B, 2C, 3A, 3B, 3C, and 3D) (Fig. 1*A*). Like Saffold virus, UC1 encodes an L protein containing a zinc finger, an acidic domain, and a partially deleted Ser/Thr-rich domain (22, 23) and potentially encodes a severely truncated L* protein that begins with an ACG codon rather than AUG (22, 23) [supporting information (SI) Fig. S1*A*].

In cardioviruses, the surface loops CD of VP1 and EF of VP2 are exposed on the capsid surface and are thought to be involved in host cell tropism and viral pathogenesis (24). These loops are the regions of greatest divergence between UC1 and the other cardioviruses, including Saffold virus (Fig. S1*B*). Between UC1 and Saffold virus, there is 52% and 61% amino acid identity in the exposed surface loops CD and EF, respectively. The corresponding identities (29% and 24%) are much lower between UC1 and the rodent cardioviruses.

Comparison of UC1 Amino Acid Sequence with Other Cardioviruses. The level of divergence between the sequence of UC1 and other cardioviruses is maintained at the amino acid level. Between UC1