CDC in Atlanta released their version of the SARS genome today, 4/14/03, and the 29,727 genome for SARS is located here: http://www.cdc.gov/ncidod/sars/pdf/nucleoseq.pdf

A blast of the 27,727 nucleotides of the complete genome of SARS was conducted using the BLAST-n program located on the PubMed/Entrez website located here: http://www.ncbi.nlm.nih.gov/

This report provides a list of the relative viruses of the SARS virus as a result of the BLAST-n and a brief discussion concerning possible transmission vectors.

To understand the below BLAST-n report, these "sequences producing significant alignments" are arranged in descending order of relatedness to SARS. The viruses below are in the coronavirus group; the single closest relative virus of SARS appears to be the "rat sialodacryoadenitis coronavirus" and this is followed by several murine hepatitis virus strains.

The first and highest "match" is for Rat sialodacryoadenitis coronavirus RNA-directed RNA polymerase (pol) and appears to confirm that SARS is a single-stranded RNA virus and is in the coronavirus family tree. SARS appears to be about 87% homologous (the same) as the Rat sialodacryoadenitis coronavirus RNA-directed RNA. But it is not 100% the same.

Next, you will see several murine hepatitis virus strains that are showing homology to SARS. SARS shows between 85% to 95% sequence homology with Murine hepatitis virus strain ML-10, complete genome. But it is not 100% the same.

Other murine/mouse hepatitis virus strains showing sequence homology to SARS include:

- Mouse hepatitis virus strain MHV-A59 C12 mutant, complete genome (about 85% to 95% homology)
- Mouse hepatitis virus RNA for viral polymerase open reading frame 1b (again about 85% to 95%)
- Murine coronavirus open reading frame 1a (gene 1), complete cds and open reading frame 1b (gene 1), 3' end (about 85% to 95% homology)
- And there are others that you can see below.

The closest human virus showing sequence homology to SARS is Human coronavirus (strain OC43) RNA-directed RNA polymerase (pol) gene, partial cds, which is showing about an 80% to 93% sequence homology to SARS. It is not 100%.

This is then followed by several bovine coronavirus sequences which show between 80% to 93% sequence homology to SARS. It appears the Quebec strain of bovine coronavirus has highest homology to SARS.

SARS is a new virus in the coronavirus family tree. It is not showing sufficiently high sequence homology with any other coronavirus to say that it is one of the currently known coronaviruses.

SARS also has sequence homology (between about 84% and 93% homology) with avian bronchitis virus. SARS also shows some very slight similarity to human coronavirus 229E, human astrovirus, and Influenza Type A (which is a orthomyxovirus). There are other parts of SARS that are completely unknown DNA. SARS appears to possibly have an avian nucleocapsid in addition to its other bits-and-pieces of different-species coronaviruses. More work is necessary on this.

It is probably prudent to consider SARS being transmissible in ways similar to the mouse/rat coronaviruses. I will discuss this later on.

The BLAST-n results:

Sequences producing significant alignments:	Score (bits)	E Value
gi|4927032|gb|AF124990.1|AF124990 Rat sialodacryoadenitis c...	103	3e-19
gi|7769351|gb|AF208067.1|AF208067 Murine hepatitis virus st...	92	1e-15
gi|2641127|gb|AF029248.1| Mouse hepatitis virus strain MHV-...	92	1e-15
gi|58974|emb|X51939.1|COMHVPOL Mouse hepatitis virus RNA fo...	92	1e-15
gi|331851|gb|M55148.1|MHVGENE1 Murine coronavirus open read...	92	1e-15
gi|6625759|gb|AF201929.1|AF201929 Murine hepatitis virus st...	82	1e-12
gi|7739593|gb|AF207902.1|AF207902 Murine hepatitis virus st...	82	1e-12
gi|7769340|gb|AF208066.1|AF208066 Murine hepatitis virus st...	82	1e-12
gi|13752444|gb|AF353511.1|AF353511 Porcine epidemic diarrhe...	80	5e-12
gi|4927030|gb|AF124989.1|AF124989 Human coronavirus (strain...	76	7e-11
gi|18033971|gb|AF391542.1| Bovine coronavirus isolate BCoV-...	72	1e-09
gi|15077808|gb|AF391541.1| Bovine coronavirus isolate BCoV-...	72	1e-09
gi|17529670|gb|AF220295.1| Bovine coronavirus strain Quebec...	68	2e-08
gi|4927028|gb|AF124988.1|AF124988 Porcine hemagglutinating ...	68	2e-08
gi|4927022|gb|AF124985.1|AF124985 Bovine coronavirus RNA-di...	66	7e-08
gi|29293452|gb|AY223860.1| Avian infectious bronchitis viru...	64	3e-07
gi|7767411|gb|AF203002.1|AF203002 Avian infectious bronchit...	64	3e-07
gi|8439045|emb|AJ278334.1|AIN278334 Avian infectious bronch...	64	3e-07
gi|6689853|gb|AF111996.1|AF111996 Turkey coronavirus strain...	64	3e-07
gi|1853990|gb|U52598.1|AIU52598 Avian infectious bronchitis...	64	3e-07
gi|292963|gb|L06251.1|IBAHYPVARA Avian infectious bronchiti...	64	3e-07
gi|292951|gb|M95169.1|IBACGB Avian infectious bronchitis vi...	58	2e-05
gi|12965364|gb|AF322368.2|AF322368 Avian infectious bronchi...	58	2e-05
gi|7767423|gb|AF203007.1|AF203007 Avian infectious bronchit...	58	2e-05
gi|8439048|emb|AJ278338.1|AIN278338 Avian infectious bronch...	58	2e-05
gi|8439047|emb|AJ278337.1|AIN278337 Avian infectious bronch...	58	2e-05
gi|8467929|emb|AJ278336.1|AIN278336 Avian infectious bronch...	58	2e-05
gi|8439046|emb|AJ278335.1|AIN278335 Avian infectious bronch...	58	2e-05
gi|458734|emb|Z30541.1|AIBVCG Avian infectious bronchitis v...	58	2e-05
gi|13397900|emb|AJ271965.2|TGA271965 Transmissible gastroen...	58	2e-05
gi|14253129|emb|AJ311362.1|IBR311362 Avian infectious bronc...	58	2e-05
gi|14149032|emb|AJ311317.1|IBR311317 Avian infectious bronc...	58	2e-05
gi|1418973|emb|Z69629.1|IBVCD61 Infectious bronchitis virus...	58	2e-05
gi|683720|emb|Z34093.1|TGVPOLL Transmissible gastroenteriti...	58	2e-05
gi|6689855|gb|AF111997.1|AF111997 Turkey coronavirus strain...	58	2e-05
gi|2062322|gb|U49858.1|AIU49858 Avian infectious bronchitis...	58	2e-05
gi|806411|gb|U04804.1|AIU04804 Avian infectious bronchitis ...	58	2e-05
gi|1853993|gb|U52601.1|AIU52601 Avian infectious bronchitis...	58	2e-05
gi|1853991|gb|U52599.1|AIU52599 Avian infectious bronchitis...	58	2e-05

gi|1853989|gb|U52597.1|AIU52597	Avian infectious bronchitis...	58	2e-05
gi|1853988|gb|U52596.1|AIU52596	Avian infectious bronchitis...	58	2e-05
gi|1853987|gb|U52595.1|AIU52595	Avian infectious bronchitis...	58	2e-05
gi|1853986|gb|U52594.1|AIU52594	Avian infectious bronchitis...	58	2e-05
gi|808698|gb|M21515.1|IBASPMNCF	Avian infectious bronchitis...	58	2e-05
gi|13171067|emb|AJ310642.1|TCO310642	Turkey coronavirus gen...	58	2e-05
gi|292965|gb|L06253.1|IBAHYPVARC	Avian infectious bronchiti...	58	2e-05
gi|292964|gb|L06252.1|IBAHYPVARB	Avian infectious bronchiti...	58	2e-05
gi|292949|gb|M28565.1|IBABEAU	Avian infectious bronchitis v...	58	2e-05
gi|331170|gb|M94356.1|IBAORFAB	Avian infectious bronchitis ...	56	7e-05
gi|1853992|gb|U52600.1|AIU52600	Avian infectious bronchitis...	56	7e-05
gi|12082738|gb|AF304460.1|AF304460	Human coronavirus 229E, ...	54	3e-04
gi|59490|emb|X69721.1|HCVORF1AB	Human coronavirus 229E mRNA...	54	3e-04
gi|28274445|gb|AY189157.1|	Avian infectious bronchitis viru...	50	0.004
gi|27803883|gb|AY180958.1|	Avian infectious bronchitis viru...	50	0.004
gi|11038441|gb|AF288146.2|AF288146	Avian infectious bronchi...	50	0.004
gi|4454355|emb|AJ011482.1|TGA011482	Porcine transmissible g...	50	0.004
gi|58986|emb|X58001.1|CORPS12A	Infectious bronchitis virus ...	50	0.004
gi|58959|emb|X04723.1|COIBVSP2	Infectious bronchitis virus ...	50	0.004
gi|4972607|gb|AF094817.1|AF094817	Avian infectious bronchit...	50	0.004
gi|4972605|gb|AF094815.1|AF094815	Avian infectious bronchit...	50	0.004
gi|4972604|gb|AF094814.1|AF094814	Avian infectious bronchit...	50	0.004
gi|806409|gb|U04739.1|AIU04739	Avian infectious bronchitis ...	50	0.004
gi|292967|gb|M28566.1|IBAMPUP	Avian infectious bronchitis v...	50	0.004
gi|27357178|gb|AY167585.1|	Porcine epidemic diarrhea virus ...	48	0.017
gi|8671364|emb|Y15937.2|SACAPSID	Sheep astrovirus, complete...	48	0.017
gi|4927034|gb|AF124991.1|AF124991	Turkey coronavirus RNA-di...	48	0.017
gi|4927024|gb|AF124986.1|AF124986	Canine coronavirus RNA-di...	48	0.017
gi|3046973|gb|AF056197.1|AF056197	Feline astrovirus capsid ...	48	0.017
gi|13378216|gb|AY024337.1|	Avian infectious bronchitis viru...	46	0.067
gi|13377886|gb|AF334685.1|AF334685	Avian infectious bronchi...	46	0.067
gi|6425132|gb|AF201930.1|AF201930	Avian infectious bronchit...	46	0.067
gi|9719315|gb|AF207551.1|AF207551	Sialodacryoadenitis virus...	46	0.067
gi|58951|emb|X15832.1|COIBVPEP	Infectious Bronchitis Virus ...	46	0.067
gi|453423|emb|X73559.1|MHVORF	MHV-A59 gene 1 and ORF1a	46	0.067
gi|58988|emb|X58003.1|CORPS12B	Infectious bronchitis virus ...	46	0.067
gi|4972606|gb|AF094816.1|AF094816	Avian infectious bronchit...	46	0.067
gi|1086958|gb|S79187.1|S79187	S2=glycoprotein [porcine hema...	46	0.067
gi|406193|dbj|D13096.1|CCOINSAVC	Canine coronavirus (CCV) g...	46	0.067
gi|21666542|gb|AF395735.1|	Human astrovirus type 3 strain H...	44	0.26
gi|20340264|gb|AF500215.1|	Porcine epidemic diarrhea virus ...	44	0.26
gi|14572176|gb|AF248738.2|AF248738	Human astrovirus type 7 ...	44	0.26
gi|4731637|gb|AF141381.1|AF141381	Human astrovirus putative...	44	0.26
gi|13785563|gb|AF257226.1|AF257226	Human astrovirus type 2 ...	44	0.26
gi|8670989|emb|Y08632.2|HAS7CAP	Human astrovirus type 7 gen...	44	0.26
gi|1617049|emb|Y08629.1|HAS3CAP	Human astrovirus type 3 gen...	44	0.26
gi|1617047|emb|Y08628.1|HAS2CAP	Human astrovirus type 2 gen...	44	0.26
gi|7595820|gb|AF239985.1|AF239985	Avian infectious bronchit...	44	0.26
gi|306320|gb|L06802.1|ATVCAPSID	Human astrovirus capsid pro...	44	0.26
gi|4325030|gb|AF117209.1|AF117209	Human astrovirus type 3 c...	44	0.26
gi|348158|gb|L13745.1|HUANSSPS	Human astrovirus serotype 2,...	44	0.26
gi|17223874|gb|AY060045.1|	Influenza A virus (A/SW/OH/7802/...	42	1.0
gi|17223872|gb|AY060044.1|	Influenza A virus (A/SW/NE/18339...	42	1.0
gi|17223846|gb|AY060031.1|	Influenza A virus (A/SW/MN/12883...	42	1.0
gi|21666548|gb|AF395738.1|	Human astrovirus type 8 strain H...	42	1.0
gi|21666546|gb|AF395737.1|	Human astrovirus type 5 strain H...	42	1.0
gi|21666537|gb|AF395733.1|	Human astrovirus type 1 strain H...	42	1.0

gi|18476472|gb|AY052786.1|	Yellow head virus ORF1a polyprot...	42	1.0
gi|15266494|gb|AY044186.1|	Avian infectious bronchitis viru...	42	1.0
gi|331846|gb|M32789.1|MHVE2GLY	Murine hepatitis virus E2 gl...	42	1.0
gi|561671|gb|U14646.1|MHU14646	Murine hepatitis virus S gly...	42	1.0

Possible Disease-transmission information:

Lab Anim Sci 1992 Aug;42(4):344-6

Transmission of sialodacryoadenitis virus (SDAV) from infected rats to rats and mice through handling, close contact, and soiled bedding.

La Regina M, Woods L, Klender P, Gaertner DJ, Paturzo FX.

Department of Comparative Medicine, St. Louis University School of Medicine, MO 63104.

Thirty mice and six rats were exposed through handling, soiled bedding, or close contact to rats previously inoculated with sialodacryoadenitis virus (SDAV). All exposed rats developed coronaviral antibody without clinical signs or lesions of SDAV infection. Exposed mice had no lesions or clinical signs of coronavirus infection. Mice exposed by handling or by soiled bedding did not develop coronavirus antibody. Two of 10 mice exposed to SDAV-inoculated rats by close contact were coronavirus seropositive when tested 3 weeks postexposure. SDAV-inoculated rats and mice developed coronavirus lesions and antibody. **These results suggest that rat-to-rat transmission of SDAV is likely via fomites or handling;** however, rat-to-mouse transmission is unlikely when animals are housed and husbanded using modern techniques. Results also suggest that coronavirus antibody in mice is due to exposure to mouse coronavirus and not to rat coronaviruses.

PMID: 1331604

Lab Anim Sci 1985 Apr;35(2):129-34

Epizootiological observations of natural and experimental infection with sialodacryoadenitis virus in rats.

Bhatt PN, Jacoby RO.

The epizootiology of sialodacryoadenitis (SDA) was studied in experimentally and naturally infected rats. **The infectivity of SDA virus (SDAV) in intranasally infected rats was lost by seven days after infection as determined by contact transmission.** After experimental infection, SN antibody appeared earlier and titers were detectable longer than CF antibody. The prevalence of SN antibody-positive rats in naturally infected colonies remained high, whereas an increase in the prevalence of CF antibody-positive rats appeared to coincide with the introduction or resurgence of SDAV. A SDAV-free colony was established by allowing recovered dams to litter in a separate room. A spontaneous cessation of SDAV

infection also was observed in an enzootically-infected colony. **Clinical observations indicated that SDA can occur as a mild or asymptomatic disease, and that its clinical expression may vary from one inbred strain to another.**

PMID: 2987613

Lab Anim Sci 1990 Jul;40(4):363-6

Infection of SDAV-immune rats with SDAV and rat coronavirus.

Weir EC, Jacoby RO, Paturzo FX, Johnson EA.

Section of Comparative Medicine, Yale University School of Medicine, New Haven, CT 06510.

Infection of rats with sialodacryoadenitis virus (SDAV) or rat coronavirus (RCV) is acute and self-limiting, and elimination and control of either virus is based on the assumption that recovered rats are immune to reinfection. To test this hypothesis, we examined whether SDAV-immune rats could be infected with RCV or reinfected with SDAV. Sprague Dawley (SD) rats were inoculated intranasally with SDAV or with culture medium alone and serial SDAV antibody titers were obtained. Eleven months after inoculation, when antibody titers had stabilized, SDAV-immune and nonimmune rats were challenged with SDAV or RCV, and euthanatized 3 or 6 days later. **SDAV-immune rats challenged with SDAV or RCV manifested acute rhinitis associated with virus antigen by 3 days after inoculation, but no lesions or antigen were subsequently found in the lower respiratory tract, salivary glands or lacrimal glands. There was also a marked anamnestic increase in antibody titer by 6 days after challenge. SDAV-immune rats challenged with SDAV or RCV also transmitted infection to nonimmune cage mates. This study indicates that 11 months after primary infection with SDAV, rats can be infected with SDAV or RCV, but that the severity of disease is significantly reduced.**

PMID: 2166861

This last article above suggests, assuming that SARS is similar to rat sialodacryoadenitis virus, that humans can be reinfected with the virus and there is not a permanent complete immunity to the disease. Later infections are not as severe as primary infection to rats, but rats that have recovered can still get re-infected and can transmit the virus to non-infected/nonimmune cage mates. It should be understood, however, that although these coronaviruses are antigenically closely related, they are biologically different viruses and disease patterns are different – no one can say definitively at this time how SARS is transmitted.

Reason would suggest it may be transmitted in ways similar to rat sialodacryoadenitis virus – but this is, at this time, speculative.

Relative to persistent infection, there seems to be some probable good news:

Am J Vet Res 1984 Oct;45(10):2077-83

Sialodacryoadenitis in the rat: effects of immunosuppression on the course of the disease.

Hanna PE, Percy DH, Paturzo F, Bhatt PN.

Eight-week-old outbred male and female Crl:CD(SD)BR rats were treated with prednisolone (PR) or cyclophosphamide (CY) and were inoculated intranasally with sialodacryoadenitis (SDA) virus. The course of the disease was compared with nonimmunosuppressed, SDA virus-inoculated rats of the same stock. Criteria used to compare SDA in the 3 groups, included histologic changes in salivary and lacrimal glands, immunofluorescent microscopy of paraffin-embedded tissues, serum amylase levels, and antibody response. Based on these criteria, there was little detectable difference in the course and intensity of SDA in PR-treated and nonimmunosuppressed rats. In CY-treated rats, there was a delay in the onset of SDA, in the appearance of inflammatory cells in affected glands, and in the reparative process in the salivary and lacrimal glands. Viral antigen persisted longer in CY-treated rats than in PR-treated and nonimmunosuppressed rats. Antibody to SDA virus was not detected in CY-treated rats. The efficacy of immunosuppression by PR and CY was confirmed by the sheep erythrocyte agglutination procedure performed in selected rats. Male and female rats of the same strain were immunosuppressed beginning 4 weeks after inoculation with SDA virus to produce recrudescence of the disease. Histologic examination of salivary and lacrimal glands, immunofluorescent microscopy, serum amylase values, and viral isolation studies did not reveal evidence of reactivation of a persistent viral infection or viral shedding. **Based on these studies, there is no evidence that SDA virus may persist as an inapparent infection after recovery from the disease.**

PMID: 6208823

It would appear that SARS may not cause a persistent infection. This is good news.

Summary of findings as of 4/14/03 in this report:

1. SARS genome has been published by CDC.
2. SARS appears to be a new coronavirus.
3. SARS appears possibly similar to rat sialodacryoadenitis (SDA) virus as well as other coronaviruses.
4. SARS-infected persons may be free of the virus once they are well (there may be no persistent infection) but they are not permanently immune to the virus, i.e., they may catch SARS again and while their symptoms the second time may be less severe than the first time, the persons may be infectious again to persons who have not been previously infected. This suggests that it will be quite difficult to manufacture a vaccine for SARS as well as to suggest that no one is permanently immune to the disease even if they have recovered from it.
5. SARS may exist in persons as an asymptomatic disease.
6. Much scientific work is necessary to understand this disease.

It will be a challenge to determine how to minimize infection numbers given that (a) a person may possibly be asymptomatic but infectious; (b) a person may have the disease and get over it but then may catch the disease again and may, again, transmit it to non-infected persons; (c) when there is a 4% mortality rate and, (d) vaccine development may be extremely difficult given that, in rats, a similar disease exists but infected rats do not appear to develop permanent immunity against the similar disease.

While it is still very early in the entire SARS science, if the above are true and the data from rat sialodacryoadenitis virus transmission apply to SARS, then SARS is here to stay and may spread over the globe again-and-again.

Let’s hope this analysis is wrong.