After the discovery

Thus, when

FIV test

IDEXX FIV ELISA positive

ELISA tests with the

Shortly thereafter they licensed

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14

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1908.

and with erythroid leukemia of chickens in

1904

1870.

Retrovirus-associated diseases of animals have been known for almost 2 centuries.1 Pulmonary adenocarcinoma in sheep was first reported in 1825 and bovine leukemia was described in 1870.2,3 Transmissible “filterable agents” were associated with equine infectious anemia in 1904 and with erythroid leukemia of chickens in 1908.4,5 The causative agents for these diseases were identified as retroviruses decades later. In fact, Payton Rous, who proposed the filterable agent for avian leukemia, was ridiculed for his hypothesis but later was awarded the Nobel Prize for the discovery. In the early 1970s, as a young Post Doctoral Fellow at Memorial Sloan Kettering Cancer Center, I was fortunate to have met Dr. Rous, then in his late 80s, who was still brilliant and a most gracious scientist interested in our work on the feline leukemia virus (FeLV). The recognition of retroviruses as tumor-inducing agents in animals revealed some fundamental aspects of the cellular mechanisms of disease and led to their designation as “RNA tumor viruses” at a Cold Spring Harbor Laboratory Meeting.6 At this meeting, I presented our work on the pathogenesis of FeLV and feline sarcoma virus (FeSV) diseases.7

Retroviruses are enveloped viruses, with single-stranded RNA genomes, which attach to cells via specific cell surface receptors. After entry into a cell, retroviruses uncoat their RNA genomes and reverse transcribe their viral RNA and integrate the DNA product into the cellular chromosomal DNA. The previous classification of retroviruses was based on disease association or morphological features. However, the current classification is based on the genetic relatedness of the RT protein and distinguishes seven genera.1

Feline Retroviruses:
The FeLV was discovered in Scotland by William Jarrett and his colleagues in 1964. At that time all retroviruses were thought to be endogenous viruses that were only transmitted genetically (vertically). However in 1973, using the FeLV IFA test (Figure 1), we demonstrated that FeLV is transmitted contagiously amongst pet cats living in our households.8

Figure 1 FeLV: negative, and positive IFA tests.

This observation was the first conclusive proof that any retrovirus was transmissible by contagious means, and changed the prevailing concepts of these viruses. We then developed a FeLV infection prevention program based on a simple blood test.9 By the mid-1970s, along with Dr. Max Essex’s group at Harvard, we began to observe that FeLV induced more immunosuppressive and cyto-reductive diseases than leukemia.10-12 Thus, when the AIDS epidemic began in the early 1980s, Dr. Essex and I were invited to national and international meetings where we presented papers suggesting that the likely etiology of AIDS was a human retrovirus since similar syndromes had been reported by our laboratories in pet cats infected with FeLV, a retrovirus of cats.6,7,11 After the discovery of the HIV-1 Lentiretrovirus etiology of AIDS (Figure 2) we and others began to look for cats with immunosuppressive diseases in the quest to isolate a similar feline lentivirus.13 With the help of a cattery owner in Petaluma, California, Dr. Neils Pedersen’s laboratory isolated the first feline Lentiretrovirus (FIV) from a cat with feline AIDS.14 We were able to isolate FIV from a cat from New York City about 6 months after the original FIV isolation. However, the University of California had obtained an FIV patent covering the virus and any test method or vaccination.15 Shortly thereafter they licensed exclusive FIV test rights to IDEXX Laboratories. The exclusive license excluded all other testing laboratories and veterinary biological companies from developing an FIV test, but more significantly, IDEXX bundled their FIV ELISA test with their FeLV ELISA test which effectively crippled competition of other FeLV tests. We developed an accurate IFA test for FIV antibodies (Figure 3), and a confirmatory western immunoblot (WB) test (Figure 4), using our FIV isolate, but we were prevented from offering the tests to veterinarians.

Figure 3

IFA FIV antibody test. FIV infected cells fluorescence strongly whereas the uninfected cells are negative.

Figure 4

Western immunoblot for FIV antibodies. Lane 1: ELISA+ WB+; Lane 2 and 3: ELISA+ WB+, C= Control WB+. The WB is the confirmatory test for HIV ELISA positive tests of people and FIV ELISA positive tests of cats.

Had there not been an exclusive FIV test license there would have been more competition, lower FIV test costs, and more widespread confirmation of in hospital Snap® IDEXX FIV ELISA positive tests. On June 2, 2009 the patent protection ended and several laboratories and manufacturers will now probably offer alternative FIV tests.

IDEXX FIV ELISA Test Accuracy

Several studies have been performed comparing the accuracy of the various FIV test methods.16-18 We have also compared (Table 1) in hospital performed FIV Snap® ELISA tests with the IDEXX PetChek® FIV ELISA sold to testing laboratories to our FIV WB confirmatory test.
Prevalence of FIV in Cats:
FIV prevalence in pet cats is worldwide with approximately 1-4% of healthy cats infected. The prevalence rises to as much as 15% in “sick” cats.15 The virus is spread mainly through bites and casual cohabitation, without fighting, does not spread the virus. Infected healthy cats usually remain healthy for years. We have tested 6,048 healthy pet cats from around the United States for FIV. FeLV and Bartonella and found that only 1.6% of the cats were infected with FIV, 1.3% with FeLV whereas 35% were infected with Bartonella. Since Bartonella is a zoonotic pathogen we feel that all infected healthy cats should also be tested for this important feline pathogen.

FIV-Related Viruses in the Wild Cats:
FIV related, but distinct, viruses occur in numerous wild felids and are closely related to human HIV and simian immunodeficiency virus (SIV). FIV infects a wide variety of host species including nine Felidae and one Hyaenidae species.6 These include the large African carnivores (lion, leopard, cheetah, and spotted hyena), and most of the South American felids: puma, jaguar, ocelot, margay, Geoffroy’s cat, and tigrina. Two Asian species, the Pallas’ cat and the leopard cat, are also infected with FIV.23-26 Genetic studies of the FIV strains suggest that FIV transmission between cat species has occurred in the past but is infrequent today.24 We have isolated several FIVs from pumas (puma Lentivirus-PLV). Figure 5 (right panel) shows our PLV WB assays of wild African cats.26

Confirmation of In Hospital FIV ELISA Positive Tests:
The WB is the “gold standard” test for FIV serology and various retrovirus experts recommend that all FIV ELISA positive tests be confirmed by the WB.17,21 The WB is the confirmatory test for positive HIV-1 ELISA tests in humans and for most serological tests that detect antibodies.22 Unlike the ELISA or IFA tests that result in a color change, the WB results in a profile of the antibody bands against the infecting agent. Many studies have shown that the WB test is more sensitive and specific than ELISA tests.23 However, the American Association of Feline Practitioners (AAFP) 2008 FIV recommendations state: “All positives should be confirmed by another test method.” They do not specify what test method to use.24 In fact, they refer to a publication by Dr. Julie Levy, co-chair of the AAFP panel, which concludes that the IDEXX FIV WB is not as sensitive or specific as the IDEXX FIV ELISA tests.25 This is NOT our observation, as we have documented that our FIV WB is more specific and more than 100 times more sensitive than the IDEXX FIV PetChek ELISA test (unpublished). In contrast to the AAFP recommendations, excellent FIV guidelines have been published by the European Advisory Board on Cat Diseases, a panel of 17 veterinary virus researchers. They recommend that all ELISA FIV positive tests should be confirmed by a WB.22

Table 1. Concordance of IDEXX FIV Snap** ELISA Test with Confirmatory NVL WB**

<table>
<thead>
<tr>
<th>FIV Snap*</th>
<th>Tested</th>
<th>NVL WB+</th>
<th>NVL WB-</th>
<th>% Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>196</td>
<td>133</td>
<td>62</td>
<td>68%</td>
</tr>
<tr>
<td>--</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>
| Performance *in hospital **by Nat Vet Lab  
ND= Insufficient numbers |

Table 2. Concordance of IDEXX FIV Snap** ELISA Test and IDEXX FIV PetChek** ELISA**

<table>
<thead>
<tr>
<th>FIV Snap*</th>
<th># Tested</th>
<th>*<em>Pet Check</em></th>
<th>**Pet Check--</th>
<th>% Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>185</td>
<td>175</td>
<td>10</td>
<td>95%</td>
</tr>
<tr>
<td>--</td>
<td>444</td>
<td>15</td>
<td>429</td>
<td>97%</td>
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<tr>
<td>Performance *in hospital **by Nat Vet Lab</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Concordance of PetChek*** ELISA with Confirmatory NVL WB**

<table>
<thead>
<tr>
<th>PetChek**</th>
<th># Tested</th>
<th>NVL WB+</th>
<th>NVL WB-</th>
<th>% Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>300</td>
<td>203</td>
<td>97</td>
<td>68%</td>
</tr>
<tr>
<td>--</td>
<td>2,086</td>
<td>41</td>
<td>2,045</td>
<td>98%</td>
</tr>
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* & ** Performed by Nat. Vet. Lab.

Table 4. Prevalence* of FIV, FeLV and Bartonella in 6,048 Healthy Pet Cats

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>FIV (ELISA)</th>
<th>FeLV (IFA)</th>
<th>Bartonella WB</th>
<th>% Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>--</td>
<td>0.048</td>
<td>0.048</td>
<td>0.048</td>
<td>1.6%</td>
</tr>
<tr>
<td>+</td>
<td>300</td>
<td>213</td>
<td>213</td>
<td>1.3%</td>
</tr>
<tr>
<td>arevalona WB</td>
<td>0.048</td>
<td>2,113</td>
<td>35%</td>
<td></td>
</tr>
</tbody>
</table>

* All tests performed by the National Veterinary Laboratory, Inc.

References:

For more FIV references: [www.nlm.nih.gov](http://www.nlm.nih.gov)