Canine heart disease remains an important disease entity in dogs of all ages, including those used in breeding programs. Detection of disease requires careful screening examinations and cooperation between veterinarian and breeder. If diagnosed, cardiac diseases, such as dilated cardiomyopathy, are troublesome insofar as their suspected heritability, high mortality rate, and negative effect on successful breeding programs. This presentation will discuss the current information regarding the diagnosis and treatment of the most common cardiac diseases that affect dogs, with special attention given to exciting new developments in the field of blood testing and stem cell transplantation.

Biographical Profile

**Dr. Mark A. Oyama** received his DVM degree from the University of Illinois in 1994 and after completing an internship at the Animal Medical Center in NYC and residency at the University of California at Davis, achieved Diplomate status in the Specialty of Cardiology in 1998. Dr. Oyama is currently the president-elect of the Cardiology Specialty of the American College of Veterinary Internal Medicine and is an associate professor of Cardiology at the School of Veterinary Medicine of the University of Pennsylvania. His interests are in canine mitral valve disease and dilated cardiomyopathy.

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- **360-A: Genome Expression Profiling: Canine Cardiomyopathy and Degenerative Mitral Valve Disease**
- **700-A: Widescale Genome Profiling in Great Danes with Dilated Cardiomyopathy**
- **702-A: Serotonin and Transforming Growth Factor-B Signaling in Canine Mitral Valve Disease**

Cardiology and Stem Cells – conference notes

The problems facing cardiac disease in dogs

- Mitral valve disease – in Cavaliers and other small breeds such as dachshunds
- Dilated cardiomyopathy – in Doberman Pinschers, Great Danes and Boxers
- Congenital heart disease – subaortic stenosis in Golden Retrievers and Newfoundlands

These diseases are expensive to diagnose and have limited treatments. This makes these problems quite difficult and hard to treat. Finding the root cause to these diseases is difficult and expensive as well.

Why do dogs get heart disease?

- Genetic liability or a spontaneous mutation
- Environmental conditions

Congenital heart disease – subaortic stenosis in Goldens and Newfs (polygenic)

Mitrval VD

- Cavaliers and other small breeds
- Dachs (polygenic)
DCM in dobes (autosomal dominant), GD (x linked) and boxers (autosomal dominant)

- Weakened heart muscle cells and progressive dilation of the heart
- Leads to heart failure and sudden death
- Poor appetite, exercise intolerance, abnormal heart rhythms, and fluid around the heart
- Despite with best medical efforts, very high mortality rates

How can stem cells help?

Two potential strategies – harvesting and growing new cells to implant or augmentation of what is already there

Current cardiac trials are being conducted. Most successful trials conducted are with patients with infarctions and disease caused by skemia and high cholesterol. Not necessarily genetic heart disease.

Autologous stem cells – using your own cells.

- No shortage
- No transplant rejection
- No ethical dilemmas – others’ cells or embryonic cells

Research he has performed has been on myoblast muscle cells.

- Take these skeletal muscle cells and put them into the heart. There are differences with these cells from heart cells but they can work.

How it is done

- Leg muscle biopsy, tissue is formulated and identified. It is then grown into muscle stem cells. These cells need to somehow be labeled to confirm how they work once they are implanted. Are they still around? How have they developed? Etc. They are dyed so at necropsy they can be analyzed.

- Cells need to be “purified” so only satellite (stem) cells are infused into the heart. How do we know what cells are what? Their protein must be analyzed. It is nearly impossible to get this fully pure and it is a very difficult problem to overcome. Studies show that up to 50% of the cells infused are “extra” cells and not the satellite cells.

- Cells need to be delivered. They need to spread the cells over a wide area, it needs to be through the least invasive way possible.
  - *Surgical intramyocardial injection – direct exposure of myocardial surface. Visual recognition of infarct zone. Highly invasive and since this must be done several times, there are high risks involved. Not a feasible or attractive option.
  - *Transendocardial injection – through a jugular catheter.
  - *Intracoronary injection – surgical or catheterization approach. Wide dissemination of cells. Risk of embolization. Through a femoral artery. This can allow for infusion directly into the left ventricle of the heart – directly into the DCM affected area of the heart. This placement can be confirmed through ultrasound and imaging technology.
  - *IV infusion – not as targeted, therefore not as effective.
1-3 million cells are infused. Not more than this because more cells can possibly block the heart. Cells are then absorbed by the heart area. Tested in beagles to confirm that heart cells are absorbed and this did stay in the heart (by checking for the dyed cells). This confirms that the infusion procedures do work.

Ways the transplanted cells could help to improve function
- Mature into muscle cells and help the muscle contract
- Produce and secrete beneficial local hormones that improve surrounding muscle
- Attract native stem cells (bone marrow, heart muscle) to help repair tissue
*Satellite cells do not necessarily become “heart” cells as previously thought, but it is how they affect the area that it is important.

It is now thought that a hormone is released by these cells. How can this hormone be harnessed? This needs to be studied…

Injectable stem cell activators
- Granulocyte colony stimulating factor (G-CSF)
- Mobilizes stem cells
- Injections of … improved heart failure signs and exercise ability
- Increased number of available bone marrow stem cells
- Decreased migratory cells

Future of transplantation
- Rebuilding damaged heart muscle
- Delivering local doses of medicine
- Delivering local gene therapy
  - Determine cell function and survival
  - Refine delivery techniques

Beyond Cytotherapeutics
- Gene transfer – gene therapy
- Correcting primary or secondary deficiencies of gene activity (through a virus)
- Infect heart muscle cells with a virus that contains active and healthy copies of the defective gene
  - Studies are being conducted in: MPS, muscular dystrophy and PWD DCM

While these studies are being developed we need to have:
- Better detection of disease
- Better understanding of the disease process
- Better treatments
  - New drugs
  - New technologies i.e. gene therapy