



National
Multiple Sclerosis
Society

MS Learn Online
Feature Presentation
To Repair and Protect: The Future of MS Treatments
Part One

Tracey>> Hi, I'm Tracey Kimball

Tom>> And I'm Tom Kimball. Welcome to MS Learn Online. As most of you know, multiple sclerosis attacks the central nervous system in a variety of ways.

Tracey>> And for those of us who have MS, we are always looking to the future for more and better treatment options to deal with this disease. So that's why I'm excited to introduce this three part series entitled, "To Repair & Protect: The Future of MS Treatments".

Tom>> In this series we'll learn about what is being done to protect and repair the damaged caused by MS to the central nervous system, how cell biology is advancing research into treatments for MS, and we'll get a better understanding of the types of damage caused by MS.

Tracey>> Let's watch Part One.

>>EJ Levy

HI, I'M EJ LEVY AND THIS IS MY DOG, VEGAS. EJ STANDS FOR ELISSA JOY; SOME PEOPLE DO CALL ME ELISSA. I LIVE IN NEW YORK CITY ON THE UPPER WESTSIDE.I WAS DIAGNOSED IN JANUARY OF 2002 WITH MULTIPLE SCLEROSIS.

I WAS DIAGNOSED WITH SECONDARY PROGRESSIVE.

IN APRIL, I DID MY FIRST MS WALK. I HAD 70 PEOPLE ON MY TEAM THAT YEAR. I THINK WE RAISED \$32,000.

MY FRIENDS AT BLONDIES, THIS SPORTS BAR THAT I USED TO GO TO -- WELL, I STILL GO TO NOW TO WATCH FOOTBALL ON SUNDAYS -- THEY ALL GOT TOGETHER AND DECIDED TO THROW A BENEFIT AS KIND OF A KICK-OFF FOR THE MS WALK. AND THIS YEAR, IT WILL BE OUR FIFTH ANNUAL BENEFIT AT BLONDIES.

I WAS WORKING PART-TIME AS A DEPUTY DIRECTOR OF A CHARTER SCHOOL IN THE SOUTH BRONX. I STARTED FULL-TIME, BUT AS MY MS PROGRESSED, I HAD TO GO TO PART-TIME, AND AFTER THAT, I DECIDED TO LEAVE BRONX PREP AND START MY OWN NOT-FOR-PROFIT CALLED MS HOPE FOR A CURE, AND IN OUR FIRST YEAR WE RAISED OVER A HALF A MILLION DOLLARS, AND WE'LL BE FUNDING REALLY WONDERFUL PROGRAMS AS WELL AS ONE OF THE NEW RESEARCH INITIATIVES AT THE MS SOCIETY CALLED FAST FORWARD. I THINK NOW, ALL MY ENERGY IS FOCUSED ON REALLY FINDING A CURE FOR MS, SO WHEN THE MS SOCIETY CALLED AND ASKED ME TO WORK ON THIS PROJECT, IT JUST SEEMED LIKE THE PERFECT FIT.

COME ON, LET'S GO.

SO I JUST WANTED YOU GUYS TO HAVE A CHANCE TO MEET MY FABULOUS MOM AND DAD, SUSAN AND JUDD LEVY.

>> **Judd Levy**

YOU GUYS EXCITED ABOUT MY TRIP?
VERY MUCH SO. I THINK IT'S GOING TO BE A LOT OF FUN, A LOT OF HARD WORK BECAUSE OF THE PLACES YOU'RE GOING AND THE DISTANCE, BUT I KNOW HOW YOU WERE ALWAYS EXCITED ABOUT LEARNING MORE ABOUT MS AND INCREASING YOUR KNOWLEDGE ABOUT ALL THE EXCITING THINGS THAT ARE HAPPENING AT MS, AND I'M REALLY

LOOKING FORWARD TO HEARING HOW YOU DO WHEN YOU COME BACK AND WHAT THE RESULTS ARE.

>> **Susan Levy** AND I'M HAPPY TO HAVE SOMEBODY TO GO OUT AND INTERVIEW THESE PEOPLE AND COME BACK AND BE ABLE TO EXPLAIN TO ME IN LAYMAN'S TERMS EXACTLY WHAT'S GOING ON.

>> **EJ Levy** I'M JUST SUPER EXCITED TO BE ABLE TO GO AND ACTUALLY MEET SOME OF THE RESEARCHERS AND SCIENTISTS THAT ARE WORKING ON FINDING A CURE, AND SPECIFICALLY ON FINDING WAYS TO REPAIR DAMAGE. WHEN I WAS DIAGNOSED FIVE, SIX YEARS AGO, THEY WEREN'T TALKING ABOUT THE ABILITY TO REPAIR. IT WAS, PROGRESSIVE MS MEANT YOU HAD PERMANENT DAMAGE, AND NOW, I MEAN, THEY'RE GOING TO HAVE TO TAKE THE WORD "PERMANENT" OUT, AND THAT'S FANTASTIC.

SO I'M REALLY EXCITED TO GET GOING. WE'RE GOING TO BE HEADING OFF TO SAN DIEGO AND TO CALGARY AND UP TO YALE TO INTERVIEW A BUNCH OF DIFFERENT RESEARCHERS AND SEE WHAT THEY'RE UP TO. I HAVE A FEELING THAT IT'S ALL GOING TO BE SO INSPIRING THAT EVEN IF I'M NOT FEELING GREAT, I WILL HAVE THE ENERGY TO KEEP GOING.

SO I LOOK FORWARD TO GETTING THERE AND SEEING WHAT'S HAPPENING.

HI, I'M IN SAN DIEGO AT THE 2007 NEUROSCIENCES CONVENTION WHERE 30,000 OF THE GREATEST BRAINS FROM AROUND THE WORLD ARE GATHERED TO SHARE THEIR IDEAS AND RESEARCH.

TODAY I'LL BE SPEAKING WITH TWO SCIENTISTS WHO ARE FOCUSING THEIR RESEARCH ON NERVOUS

SYSTEM REPAIR, BASICALLY FINDING WAYS TO FIX THE DAMAGE THAT IS DONE IN MS. DR. CHARLES FFRENCH-CONSTANT, THANK YOU SO MUCH FOR TAKING THE TIME TO MEET WITH ME TODAY.

>> **Dr. ffrench-Constant** IT'S A PLEASURE.

>> **EJ Levy** YOUR RESEARCH HAS TO DO WITH REPAIRING THE DAMAGE THAT OCCURS IN MS. BEFORE WE TALK ABOUT THE REPAIRING, CAN YOU EXPLAIN TO ME A LITTLE BIT ABOUT WHAT THE KIND OF DAMAGE DOES OCCUR IN MS?

>> **Dr. ffrench-Constant** YEAH, SO AS YOU KNOW, MS IS AN INFLAMMATORY CONDITION, WHERE CELLS THAT CAUSE INFLAMMATION COME OUT OF THE BLOOD INTO THE BRAIN AND ATTACK THE MYELIN AND THE CELLS THAT FORM MYELIN, WHICH ARE CALLED OLIGODENDROCYTES. NOW, THE CONSEQUENCE OF THAT IS THAT THE MYELIN SHEATH THAT SURROUNDS INDIVIDUAL NERVE FIBERS IN THE BRAIN IS DESTROYED. NOW THAT IN TURN CAUSES PROBLEMS WITH THE CONDUCTION OF NERVE IMPULSES ALONG THE NERVE FIBER, AND SO YOU GET THE SYMPTOMS OF A RELAPSE OF MS. BUT THEN GRADUALLY, OVER THE NEXT FEW DAYS AND WEEKS, THE INFLAMMATION WILL SUBSIDE AND YOU GET A REMISSION. NOW, BUT IT'S IMPORTANT TO REALIZE THAT THE REMISSION OCCURS BEFORE THE MYELIN IS REFORMED. EARLY ON IN THE COURSE OF THE DISEASE, WE KNOW THAT THE MYELIN THAT HAS BEEN DAMAGED WILL REFORM QUITE NORMALLY, AND SO EARLY ON, SOMEBODY WHO HAS AN ACUTE RELAPSE, IF YOU LOOK SOME MONTHS LATER, YOU WOULD FIND IT VERY DIFFICULT TO SEE THAT THERE WAS ACTUALLY ANY

DAMAGE AT ALL IN THEIR NERVOUS SYSTEM.

BUT GRADUALLY AS TIME GOES BY, THE REPAIR PROCESS STARTS TO FAIL, AND YOU START TO GET AXONS, OR NERVE FIBERS, WHICH ARE NO LONGER SURROUNDED BY MYELIN SHEATHS.

>> **EJ Levy** AS WE SAID EARLIER, YOUR RESEARCH HAS TO DO WITH REPAIRING, AND TO WHAT EXTENT THE MYELIN CAN ACTUALLY REPAIR ITSELF IN THE BODY. SO HOW DOES THAT WORK? HOW DOES THE MYELIN ACTUALLY REPAIR ITSELF?

>> **Dr. French-Constant** BECAUSE THE BRAIN HAS ACTUALLY GOT VERY LARGE NUMBERS OF CELLS WITHIN IT THAT HAVE THE CAPACITY TO FORM NEW OLIGODENDROCYTES, AND THIS HAS REALLY BEEN A RELATIVELY RECENT DISCOVERY IN MULTIPLE SCLEROSIS RESEARCH. AND IN FACT, AT THIS MEETING WE'RE AT NOW, THERE'S BEEN QUITE A LOT OF WORK PRESENTED ON THIS, SHOWING THAT HUGE NUMBERS OF CELLS IN THE ADULT BRAIN CAN ACTUALLY FORM NEW OLIGODENDROCYTES. WE KNOW THAT ONCE A CELL THAT'S FORMED MYELIN IS DAMAGED, IT CAN'T FORM A NEW MYELIN SHEATH; IT'S GONE. BUT WE KNOW THAT ALL OF THESE PRECURSOR CELLS, AS WE CALL THEM, CAN GENERATE NEW OLIGODENDROCYTES AND FORM NEW MYELIN SHEATHS. AND SO THERE'S THIS ENORMOUS REPAIR CAPACITY IN THE BRAIN. IT FAILS, AND WHAT WE'VE GOT TO ESTABLISH IS WHY IT FAILS AND HOW WE CAN KICK IT BACK INTO LIFE.

>> **EJ Levy** SO BASICALLY THESE CELLS THAT MAKE MYELIN ARE

DAMAGED; THEY CAN'T MAKE ANY MORE MYELIN, AND THE BRAIN, AS YOU SAID, HAS THE CAPACITY TO HAVE OTHER CELLS BECOME OLIGODENDROCYTES AND THEN MAKE THE MYELIN TO HELP THE REPAIR.

>> **Dr. ffrench-Constant** THAT'S RIGHT, BUT IN FACT ONE OF THE KEY, I THINK, ADVANCES OVER THE LAST FEW YEARS HAS BEEN THE RECOGNITION THAT OLIGODENDROCYTES CAN BE DAMAGED IN TWO BASIC WAYS. ONE SORT OF DAMAGE ACTUALLY ATTACKS THE MYELIN SHEATH; THE OTHER SORT OF DAMAGE ATTACKS THE WHOLE CELL, AND THAT'S AN IMPORTANT DISTINCTION BECAUSE IN THOSE FORMS OF MS WHERE THE MYELIN SHEATH IS ATTACKED, THE OLIGODENDROCYTES AND THEIR PRECURSORS ARE STILL HEALTHY CELLS, SO NEW MYELIN SHEATHS CAN BE FORMED. BUT IF THE DISEASE IS ACTUALLY ATTACKING THE OLIGODENDROCYTES AND THEIR PRECURSORS DIRECTLY, THEN REPAIR TENDS TO OCCUR VERY POORLY IN THOSE PATIENTS, AND ONE THEORY AS TO WHY SOME PEOPLE GET PROGRESSIVE MS QUITE QUICKLY IS BECAUSE THEY'RE ACTUALLY ATTACKING THE WHOLE CELL, WHEREAS, OTHER PEOPLE ARE JUST -- THE MYELIN SHEATH IS THE FOCUS OF THE ATTACK.

>> **EJ Levy** I KNOW ANOTHER AREA OF YOUR RESEARCH IS LOOKING AT TRANSCRIPTION FACTORS. CAN YOU TELL ME WHAT A TRANSCRIPTION FACTOR IS?

>> **Dr. ffrench-Constant** YEAH, SO WHAT WE'RE TRYING TO DO HERE IS WE'RE TRYING TO BASICALLY FIND WAYS OF

INCREASING THE REPAIR CAPACITY OF THE CELLS IN THE BRAIN. WE KNOW THAT IN PATIENTS OF OVER MANY YEARS, THE REPAIR PROCESS STARTS TO FAIL, AND IN SOME OF THOSE PATIENTS IT FAILS DESPITE THE FACT THAT THERE'S STILL LOTS OF PRECURSORS IN THE BRAIN. SO WHAT WE'VE GOT TO DO IS WE'VE GOT TO TRY AND FIND WAYS OF ACTUALLY INCREASING THE REPAIR ACTIVITY OF THOSE PRECURSOR CELLS. NOW WE KNOW THAT THE FUNDAMENTAL CONTROL MECHANISM IN A CELL TO GET IT TO BEHAVE IN DIFFERENT WAYS

IS THE WAY IT REGULATES ITS GENETIC MATERIAL, THE WAY ITS GENES MAKE PROTEINS. AND THOSE ARE CONTROLLED BY FACTORS CALLED TRANSCRIPTION FACTORS, WHICH ARE PROTEINS THAT BIND TO THE GENES AND REGULATE THEIR ACTIVITY. WE'VE IDENTIFIED 25 OR SO TRANSCRIPTION FACTORS, WHICH ARE EXPRESSED IN ASSOCIATION WITH SUCCESSFUL REPAIR, SO NOW WE HAVE A HANDLE. WE KNOW THOSE TRANSCRIPTION FACTORS ARE INVOLVED IN REPAIR. WE CAN ASK HOW DO THEY WORK, HOW CAN WE MANIPULATE THEIR BEHAVIOR, AND CAN WE USE THAT KNOWLEDGE TO DEVISE NEW TREATMENTS?

>> **EJ Levy**

NOW YOU JUST SPENT THE PAST FEW DAYS AT THIS WONDERFUL NEUROSCIENCES CONVENTION. DID YOU HEAR ANYTHING THAT WOULD BE EXCITING OR OF INTEREST TO PEOPLE WITH MS?

>> **Dr. ffrench-Constant**

WELL, WHAT'S EXCITED ME ABOUT THIS MEETING IS I THINK THAT PEOPLE ARE REALLY ASKING THE RIGHT QUESTIONS NOW. THERE'S BEEN

A LOT OF WORK EXAMINING THE MECHANISMS BY WHICH THE MYELIN SHEATH IS ACTUALLY FORMED, THE WAY THAT IT WRAPS ITSELF AROUND THE NERVE FIBERS, AND CLEARLY, THAT'S ABSOLUTELY FUNDAMENTAL FOR DEVISING STRATEGIES TO REPAIR MS. WE NEED TO KNOW HOW THAT WORKS SO THAT WE CAN DISCOVER DRUGS THAT WILL PROMOTE THE ACTIVITY. AND OVER THE LAST TEN YEARS OR SO, WE HAVEN'T REALLY BEEN ABLE TO LOOK AT THAT PROPERLY, BUT WITH THE TECHNOLOGIES THAT ARE NOW AVAILABLE, WE CAN ACTUALLY STUDY THE PROCESS OF MYELINATION PROPERLY, AND I THINK THAT WILL MAKE A BIG DIFFERENCE.

>> **EJ Levy** WELL, THANK YOU SO MUCH AND KEEP UP THE FANTASTIC WORK.

>> **Dr. ffrench-Constant** WELL, THANK YOU.

>> **EJ Levy** HI, DR. DUNCAN. THANK YOU SO MUCH FOR MEETING WITH ME TODAY. I WAS DIAGNOSED WITH MS IN 2002, SO HAVING THE CHANCE TO MEET WITH RESEARCHERS LIKE YOURSELF IS REALLY IMPORTANT TO ME. NOW I KNOW YOUR AREA OF RESEARCH IS IN NERVOUS SYSTEM REPAIR. WHY IS IT SUCH AN IMPORTANT AREA OF RESEARCH FOR PEOPLE WITH MS?

>> **Dr. Duncan** WELL, IT'S VERY IMPORTANT BECAUSE RIGHT NOW WE HAVE ABSOLUTELY NO MEANS OF PROMOTING REMYELINATION AND PROBABLY NEUROPROTECTION IN THE SPINAL CORD AND

BRAINS OF PEOPLE WITH MS, AND THERE ARE MANY OF THOSE. SO THAT'S THE GOAL, IS TO DEVISE STRATEGIES TO DO THIS.

>> **EJ Levy** NOW I KNOW THERE'S ANOTHER AREA OF RESEARCH RIGHT NOW IS IN NERVOUS SYSTEM PROTECTION; HOW DOES THAT FIT IN WITH NERVOUS SYSTEM REPAIR?

>> **Dr. Duncan** WELL, I MEAN, THEY'RE NOT MUTUALLY EXCLUSIVE, BECAUSE THE GOAL FOR MOST PEOPLE IS TO REPLACE MYELIN SHEATHS, AND IF YOU REPLACE THE MYELIN SHEATH, YOU ACTUALLY USE THIS AS A FORM OF NEUROPROTECTION. SO IT HAS TWO BENEFITS: REPLACED MYELIN RESTORES THE NERVE CONDUCTION TO THOSE NERVE FIBERS AND AXONS, AND THEN WE HOPE BY EXTENSION, IMPROVES OR RESTORES CLINICAL FUNCTION. WHILE AT THE SAME TIME THESE NERVE FIBERS THAT HAVE BEEN CHRONICALLY DEMYELINATED FOR WEEKS, MONTHS, AND YEARS ARE AT RISK OF DYING AND DEGENERATING. SO THIS CELLULAR THERAPY WILL DO JUST THAT. SO THAT'S THE ULTIMATE -- THE ULTIMATE THING TO DO IS TO BE ABLE TO REMYELINATE AND IT FORMS -- IMPROVE CONDUCTION AND NEUROPROTECTION. BUT WE HAVE TO ACKNOWLEDGE THAT THESE THERAPIES ARE GIVEN IN ADDITION TO THERAPIES THAT WILL STOP OR BLOCK ONGOING DISEASE. SO THE CURRENT DRUGS WILL BE VERY HELPFUL; NEW DRUGS WILL BE EVEN MORE HELPFUL. AND THEN THERE ARE DRUGS THAT WILL BE BOTH ANTI-INFLAMMATORY, I.E. PROTECTING AGAINST THE RELAPSES IN MS, AND ALSO HAVE NEUROPROTECTIVE PROPERTIES TOO, SO THAT'S A

COMBINED THERAPY THAT WILL FINALLY SUCCEED.

>> **EJ Levy** I KNOW YOUR TEAM WAS ALSO WORKING ON NON-
INVASIVE IMAGING TECHNIQUES SO THAT YOU CAN
SEE THE REPAIR AND THE DAMAGE THAT IS IN
PEOPLE WITH MS. WHY IS IT IMPORTANT TO BE ABLE
TO SEE THIS?

>> **Dr. Duncan** WHEN WE PUT THE CELLS IN, WE WANT TO BE ABLE
TO TRACK WHERE THEY GO, WE WANT TO SEE
WHETHER THEY STAY AT THE SITE OF
IMPLANTATION OR THEY'RE ABLE TO MIGRATE
EXTENSIVELY THROUGHOUT THE BRAIN AND
SPINAL CORD. SO WE WOULD LIKE TO BE ABLE TO
DO THIS WITH IN VIVO, IN LIVE IMAGING OF
ANIMALS, AND THEN APPLY THE SAME TECHNIQUES
TO THE HUMAN PATIENTS SO THAT WE CAN FOLLOW
IT UP, WHETHER THE CELLS HAVE MOVED,
WHETHER THEY'VE SURVIVED. THERE ARE MANY
REASONS WHY THAT WOULD BE VERY IMPORTANT,
AND THEN FINALLY WHAT YOU WOULD WANT TO
DO IS BE ABLE TO SEE THAT THE CELLS ARE MAKING
NEW MYELIN, THEY'RE REMYELINATING, SO WE
HAVE TO FOLLOW ALL THESE PARAMETERS. WE'RE
ALSO USING TECHNIQUES AT UW MADISON WHERE
WE CAN EVALUATE THE DEGREES OF
INFLAMMATION IN THE AREAS OF DAMAGE, AND
ALSO MEASURE THE NUMBERS OF AXONS, NERVE
FIBERS, THAT ARE SURVIVING, BECAUSE WE NEED
TO KNOW THE KIND OF MILIEU OF WHAT WE'RE
GOING TO PUT CELLS INTO, WHETHER IT'S A BLACK
HOLE WITH NOTHING THERE WHICH WOULD BE
WASTEFUL AND WOULDN'T WORK, OR WHETHER

THERE'S ENOUGH TISSUE SUBSTRATE THERE THAT CAN BE REPAIRED.SO IMAGING IS VERY, VERY IMPORTANT.

>> **EJ Levy** REPAIR IN MS -- I'M ASSUMING YOU'RE WORKING HARD ON THIS BECAUSE YOU BELIEVE THAT IT WILL HAPPEN. DO YOU HAVE A TIMELINE AND SOMETHING THAT WE CAN SEND OUT TO PEOPLE WITH MS TO GIVE THEM HOPE THAT THIS IS SOMETHING THAT WILL HAPPEN IN THEIR LIFETIMES?

>> **Dr. Duncan** WELL, THAT'S A VERY LOADED QUESTION. CAN I JUST SAY, BEFORE I RETIRE?

>> **EJ Levy** YES.

>> **Dr. Duncan** WE HOPE -- OUR GOAL IS, OR OUR PLAN IS PERHAPS TO INITIATE A TRIAL WITHIN A FIVE TO SIX-YEAR PERIOD. THAT NEEDS PROGRESS, A LOT OF HARD WORK, AND SOME GOOD LUCK. THERE'S A CERTAIN SLICE OF LUCK THAT YOU NEED TO HAVE EVERYTHING JUST TO WORK AND FALL INTO PLACE. I WOULD CERTAINLY SAY THAT A CELL THERAPY IN MS WILL HAPPEN WITHIN THIS DECADE. I THINK I CAN GO ON RECORD AS SAYING THAT, AND IF NOT, YOU CAN CALL ME UP IN TEN YEARS TIME AND ASK ME WHY NOT.

>> **EJ Levy** OKAY, THANK YOU SO MUCH.

WE'VE HAD A WONDERFUL DAY IN SAN DIEGO LEARNING ABOUT ALL THE ADVANCES AND RESEARCH THAT IS HAPPENING IN MS. I CAN'T WAIT

TO SEE WHAT WILL HAPPEN AT NEXT YEAR'S
MEETING.

Tracey>> I agree with EJ, I'm excited that each year brings more progress and advancement in MS research.

Tom>> Thanks to you our audience for joining us for MS Learn Online. We encourage you to join us for the next two segments of "To Repair & Protect: The Future of MS Treatments".