

SPARKING

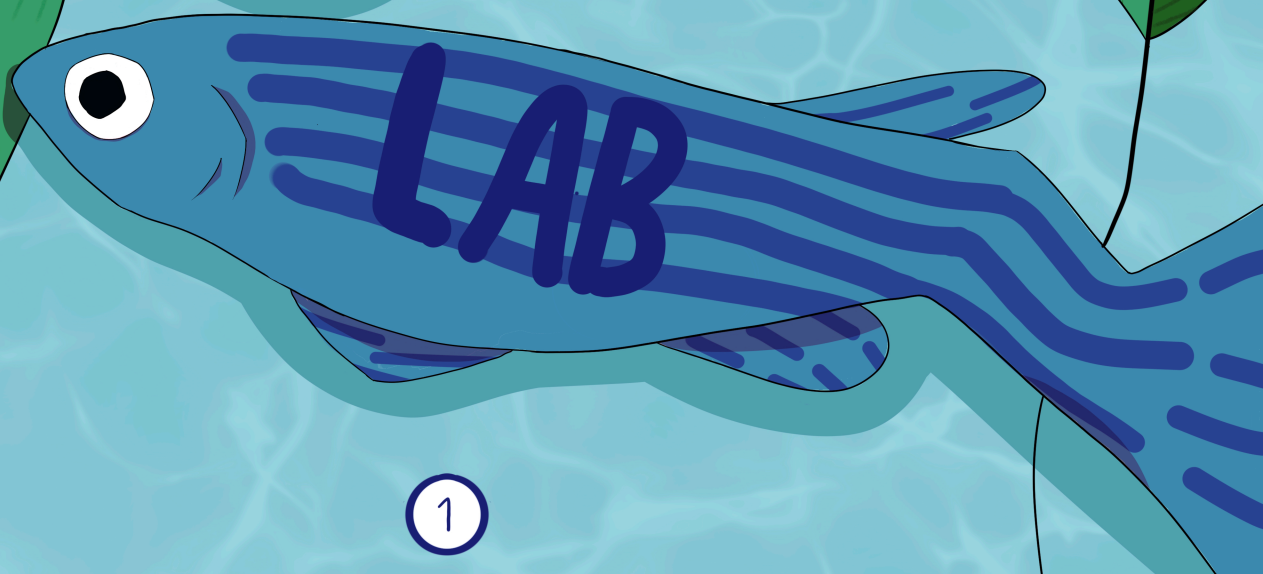


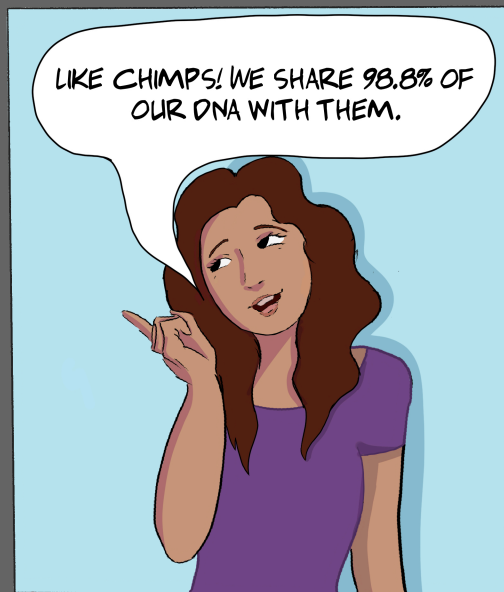
**BIOELECTRIC COMMUNICATION
DURING
ZEBRAFISH DEVELOPMENT**

LIFE

RESEARCH BY
DR. RACHEL LUKOWICZ-BEDFORD
AND ILLUSTRATED BY
BENTLEY SMALLWOOD

THANK YOU TO
UNIVERSITY
of
OREGON





UNTIL THE 1970'S CHIMPS WERE TAKEN FROM THEIR MOTHERS IN THE WILD FOR USE IN RESEARCH, WHICH DISABLED CHIMP MOTHERS, AND DISRUPTED THEIR FAMILIES AND COMMUNITIES.



MEETING CHIMPS' COMPLEX EMOTIONAL, AND SOCIAL NEEDS IN CAPTIVITY IS DIFFICULT.



BECAUSE OF THESE FACTORS, SCIENTISTS SEEK ETHICAL WAYS TO STUDY HUMAN BIOLOGY USING **MODEL ORGANISMS**: ANIMALS WITH GENETIC SIMILARITY TO HUMANS THAT ARE EASIER TO MAINTAIN IN LAB ENVIRONMENTS.

SOME OF THE MOST COMMON ORGANISMS ARE:

THE CORE FOUR

NEMATODES

PROS

- FAST DEVELOPMENT AND MATURATION
- SMALL AND INEXPENSIVE TO CARE FOR
- CONTAINS 75% OF THE SAME GENES AS HUMANS

CONS

- SIMPLE ANATOMY LACKS SOME MAMMALIAN ORGANS AND TISSUES, SUCH AS:
 - LUNGS
 - LIVER
 - KIDNEYS
 - BLOOD TRANSPORTATION SYSTEMS

PROS

- MAMMALS WITH HIGH GENETIC SIMILARITY
- VERTEBRATE

CONS

- DEVELOPS IN UTERO
- REQUIRES MORE LAB ENVIRONMENT ATTENTION
- 21 DAYS TO GIVE BIRTH
- 4-7 WEEKS TO MATURE

MICE



FRUIT

FLIES

PROS

- FAST DEVELOPMENT AND MATURATION
- SMALL AND INEXPENSIVE TO CARE FOR

CONS

- ONLY 60% OF GENE SIMILARITY TO HUMANS
- LACK MAMMALIAN ORGANS BECAUSE THEY ARE INVERTEBRATES

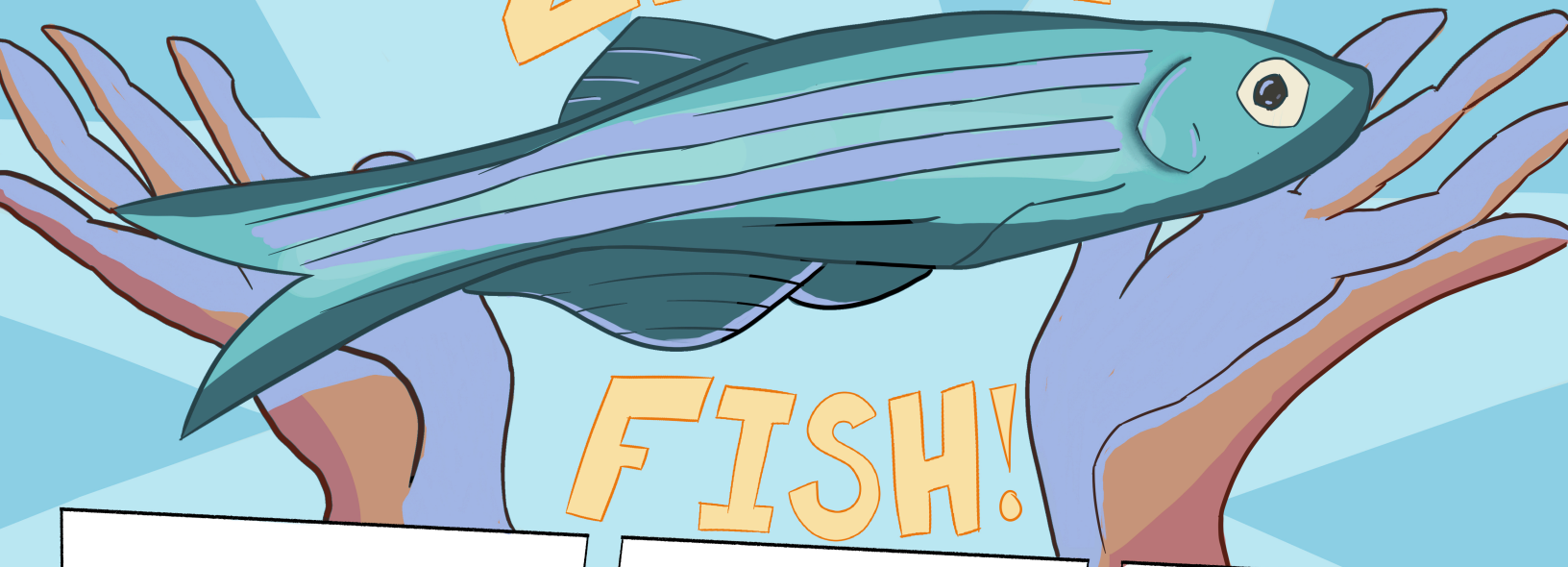
THIS IS WHY OUR MAIN CRITERIA FOR PICKING A MODEL ORGANISM ARE:

- GENETIC SIMILARITY WITH HUMANS
- QUICK DEVELOPMENT/MATURITY TIMELINE
- NUMBER OF OFFSPRING
- ABILITY TO RAISE IN A LAB ENVIRONMENT

THE FOURTH ORGANISM THAT RESEARCHERS AT THE UNIVERSITY OF OREGON DEVELOPED AS A GREAT MODEL ORGANISM TO UNDERSTAND HUMANS IS...

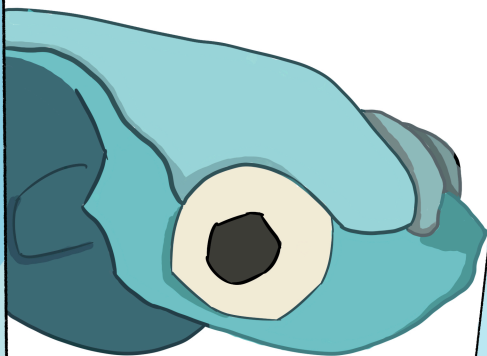


ZEBRA



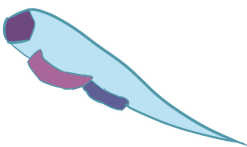
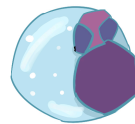
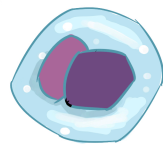
FISH!

ZEBRAFISH DEVELOP
RECOGNIZABLE TISSUES
SUCH AS BRAINS AND
HEARTS AT ONE DAY OLD!



THEY DEVELOP
OUTSIDE OF THEIR...

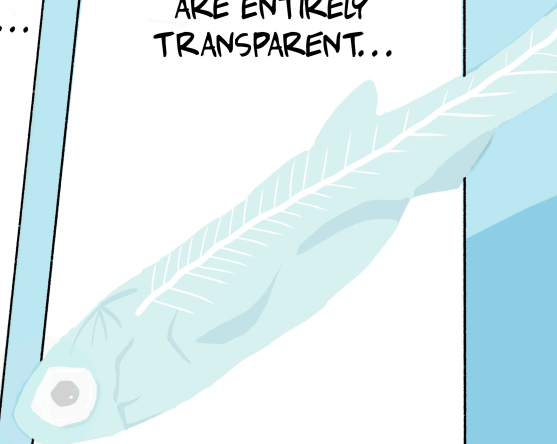
...MOTHER IN TINY,
TRANSPARENT
BUBBLES CALLED...



CHORIONS!



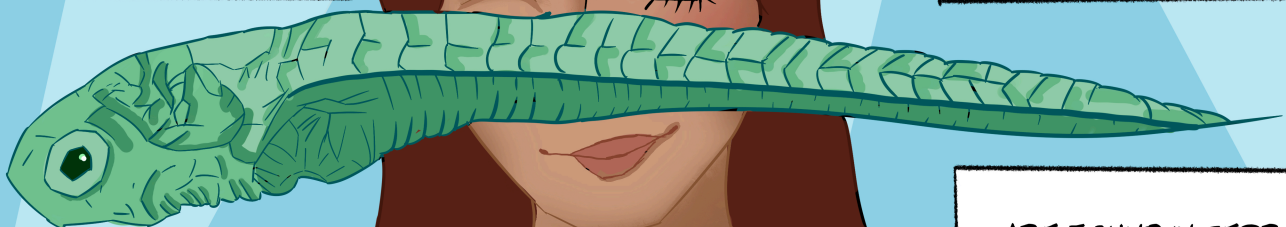
EARLY IN
DEVELOPMENT, THEY
ARE ENTIRELY
TRANSPARENT...



...MAKING IT EASY TO
OBSERVE HOW THINGS
DEVELOP

ABOUT 85% OF OUR GENES...

...INCLUDING THOSE THAT
CODE FOR DEVELOPMENT
AND DISEASES...



...ARE FOUND IN ZEBRAFISH.

SO HOW DO
RESEARCHERS USE
FISH TO UNDERSTAND
HUMANS?

ONE EXAMPLE IS THAT HUMANS
AND ZEBRAFISH SHARE SIMILAR
CELLULAR COMMUNICATION
MECHANISMS,



SENDING CELL

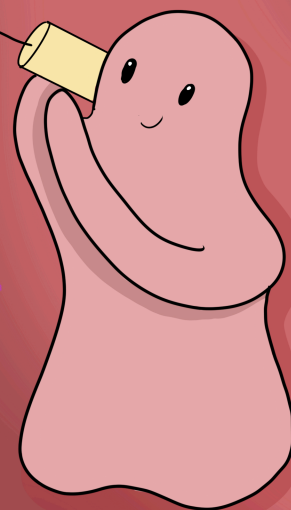
INCLUDING RELEASING
MOLECULES

Sending
molecules
your way!



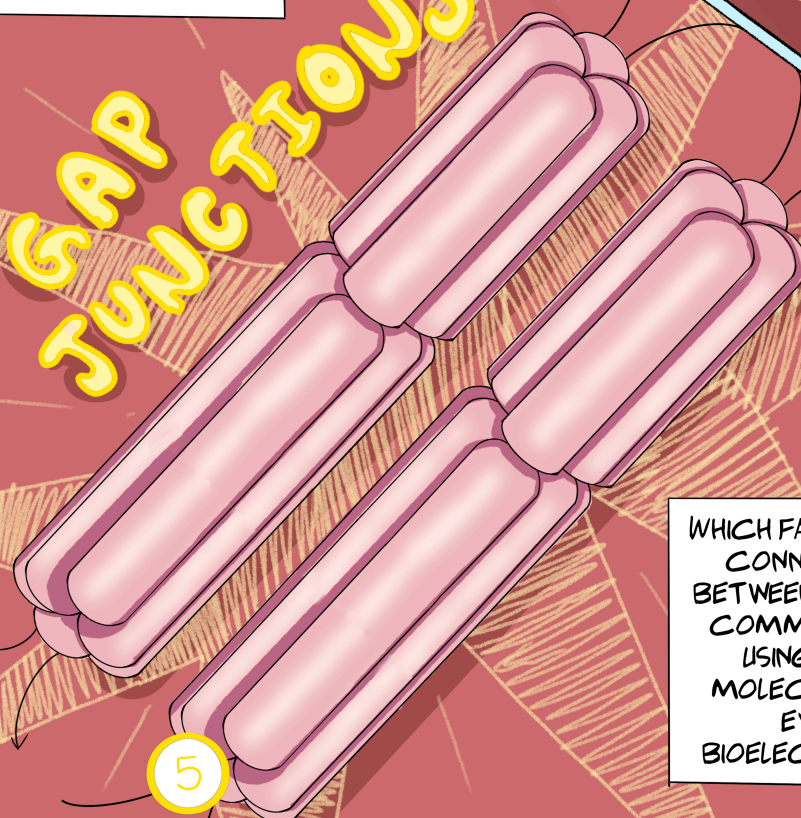
TARGET CELL

AND EXERTING
BIOCHEMICAL FORCES.

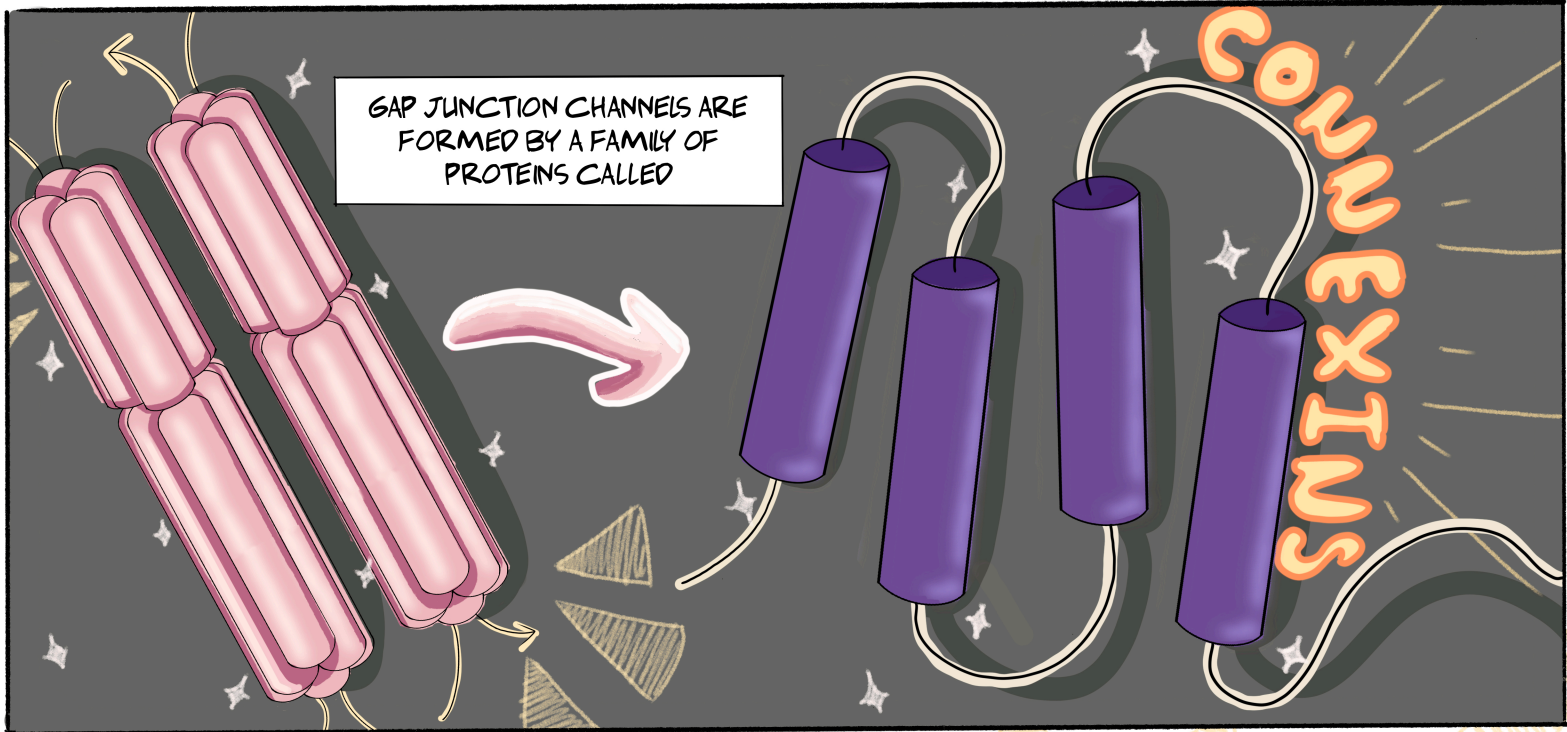


CELLS ALSO
COMMUNICATE
THROUGH
SPECIALIZED
CHANNELS CALLED

GAP JUNCTIONS



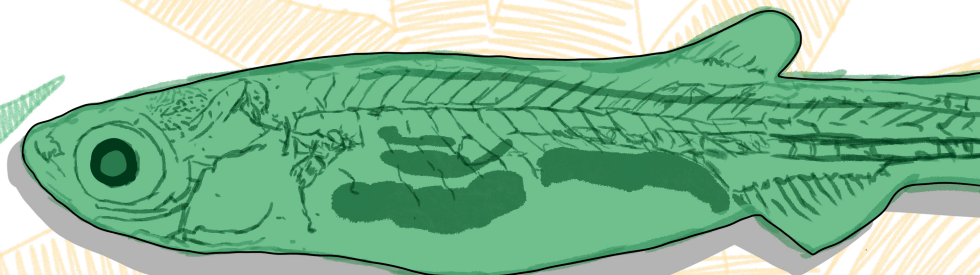
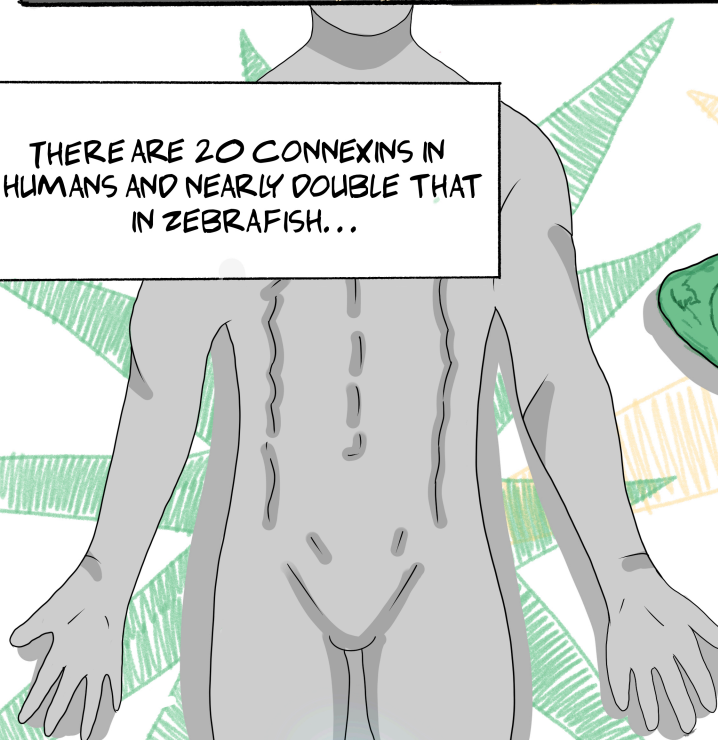
WHICH FACILITATE A
CONNECTION
BETWEEN CELLS TO
COMMUNICATE
USING SMALL
MOLECULES OR
EVEN
BIOELECTRICITY!



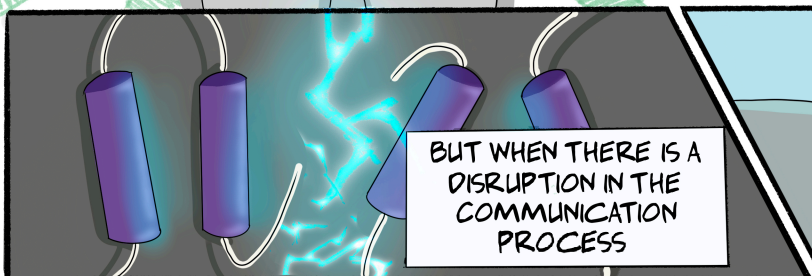
GAP JUNCTION CHANNELS ARE FORMED BY A FAMILY OF PROTEINS CALLED

CONNEXINS

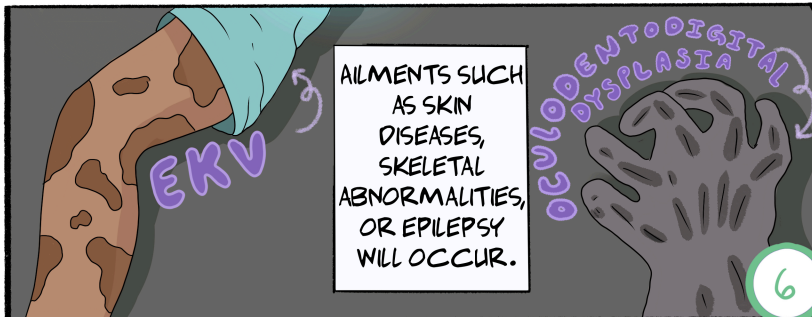
THERE ARE 20 CONNEXINS IN HUMANS AND NEARLY DOUBLE THAT IN ZEBRAFISH...



... AND IN HUMANS AND FISH, NEARLY ALL TISSUES TALK THROUGH GAP JUNCTION COMMUNICATION.

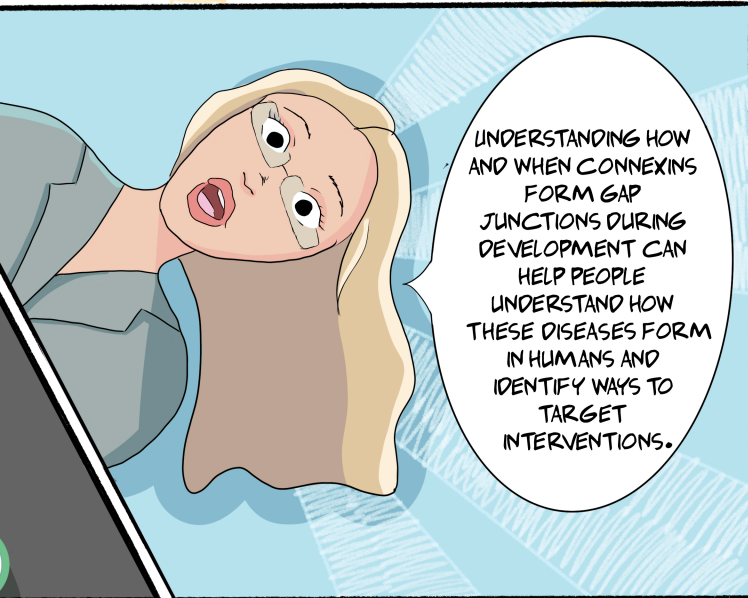


BUT WHEN THERE IS A DISRUPTION IN THE COMMUNICATION PROCESS

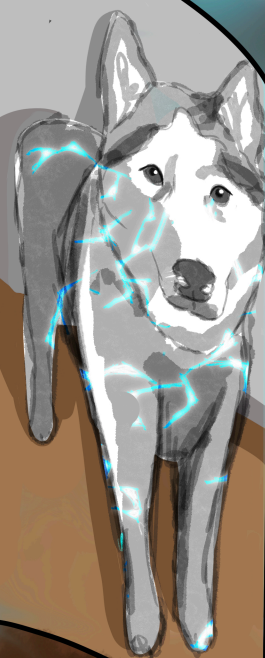
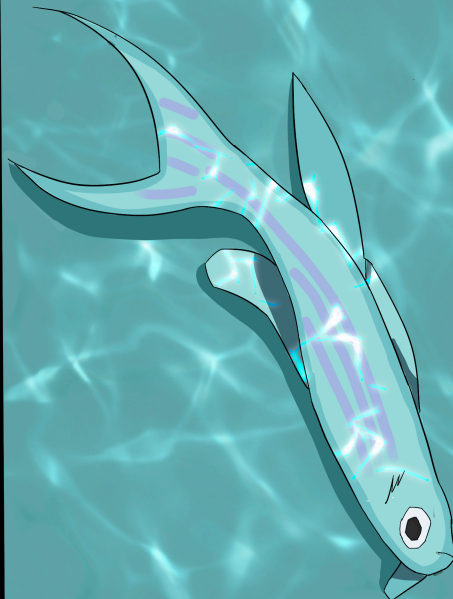
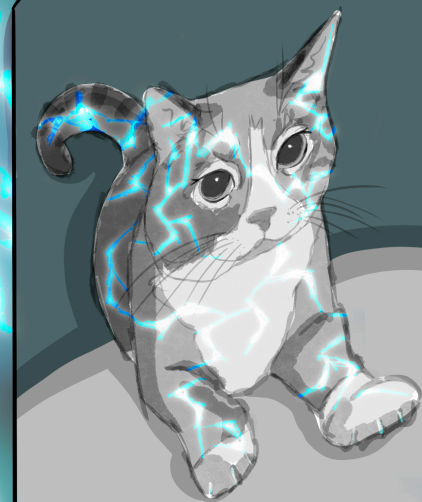


AILMENTS SUCH AS SKIN DISEASES, SKELETAL ABNORMALITIES, OR EPILEPSY WILL OCCUR.

EKG
OCULODENTODIGITAL DYSPLASIA



UNDERSTANDING HOW AND WHEN CONNEXINS FORM GAP JUNCTIONS DURING DEVELOPMENT CAN HELP PEOPLE UNDERSTAND HOW THESE DISEASES FORM IN HUMANS AND IDENTIFY WAYS TO TARGET INTERVENTIONS.



SOME OF THE MOST
IMPORTANT SIGNALS THAT PASS
THROUGH CONNEXIN-BASED GAP
JUNCTION CHANNELS ARE
CALLED BIOELECTRICITY...

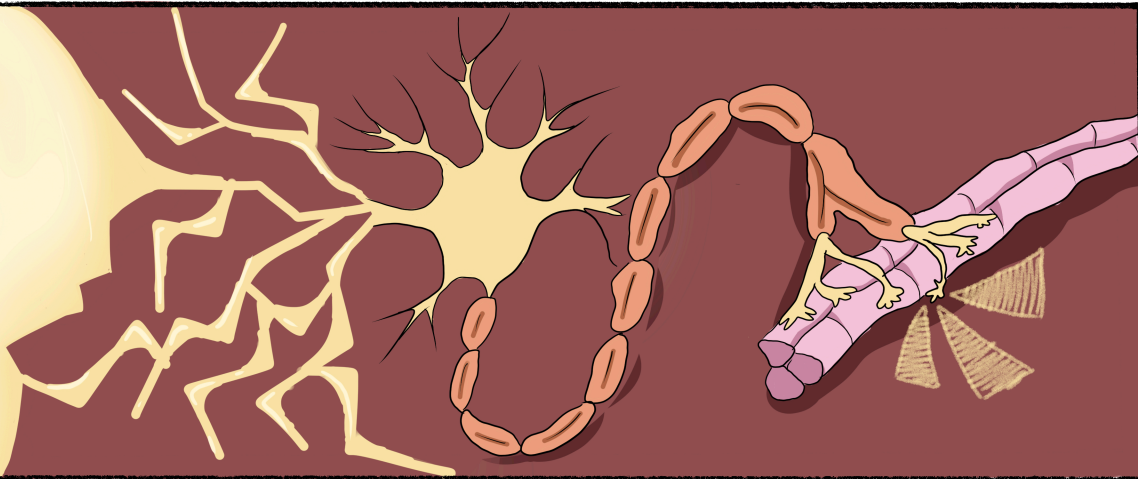
... SMALL, CHARGED
MOLECULES THAT CHANGE THE
ELECTRIC POTENTIAL OF CELLS.





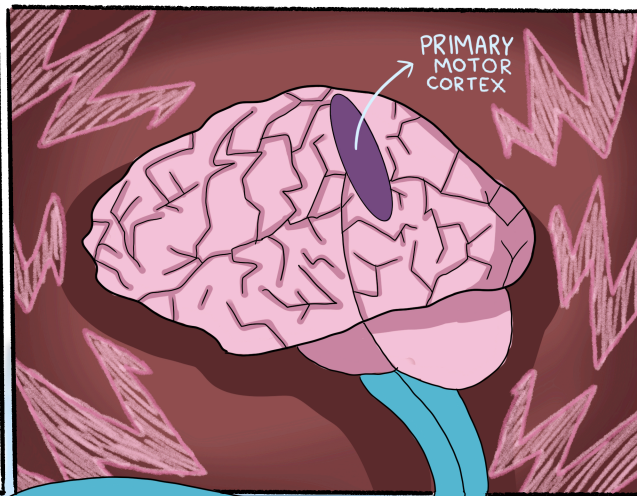
BECAUSE THERE ARE SO MANY
CONNEXINS IN HUMANS AND
ZEBRAFISH, IT IS DIFFICULT TO
FIGURE OUT WHICH ONES ARE
FORMING CHANNELS THAT
FACILITATE BIOELECTRIC
SIGNALING DURING DEVELOPMENT.

ONE WAY TO STUDY THE
ROLE OF CONNEXIN-
BASED GAP JUNCTIONS
AND THE FLOW OF
BIOELECTRICITY
DURING DEVELOPMENT
IS THROUGH THE
NEUROMUSCULAR
SYSTEM!



THE NEUROMUSCULAR
SYSTEM IS COMPOSED OF
NEURONS FROM THE
SPINAL CORD, CALLED
MOTONEURONS, THAT TALK
TO THE MUSCLES. THE
MUSCLES RESPOND BY
CONTRACTING OR
RELAXING, ALLOWING
FUNCTION AND
MOVEMENT! WE CAN USE
ZEBRAFISH TO STUDY THIS!

PRIMARY
MOTOR
CORTEX

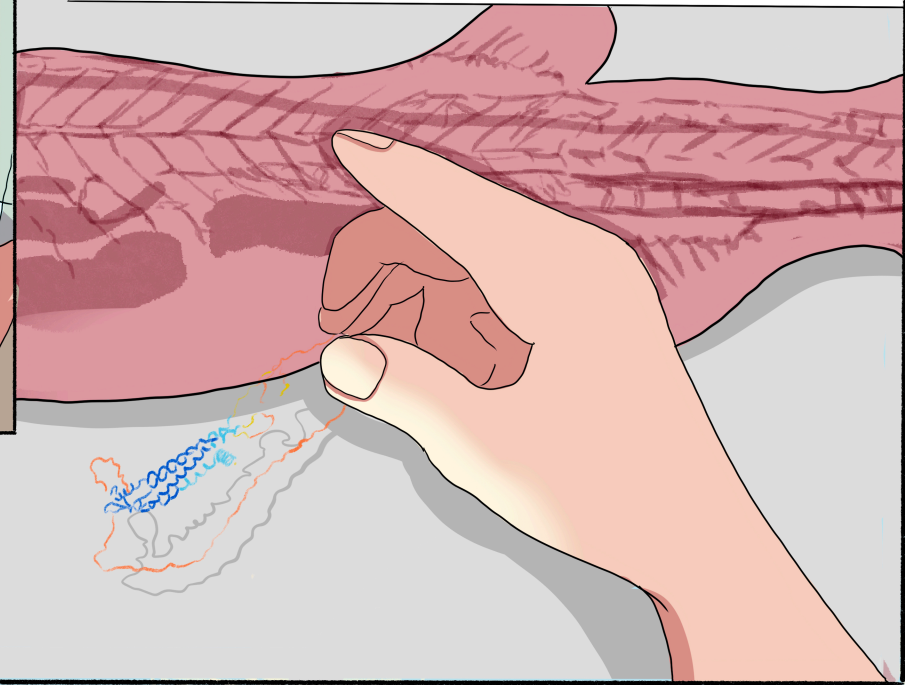
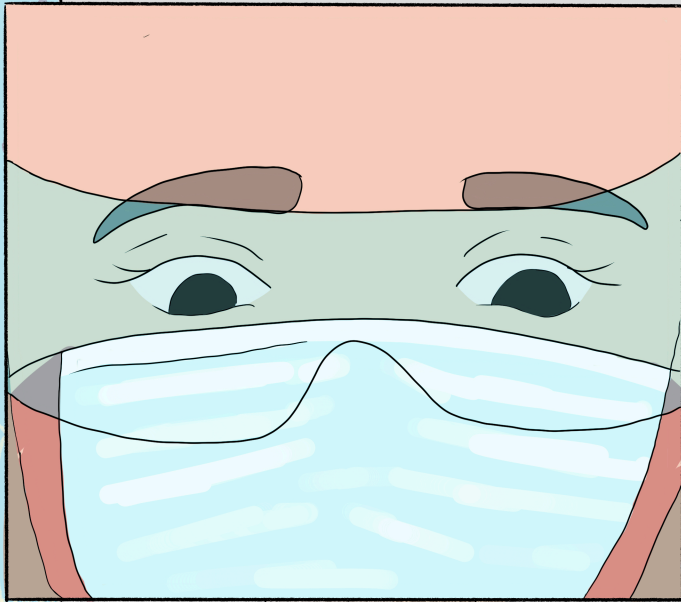


THE MOTONEURONS IN THE
SPINAL CORD CONNECT TO THE
MUSCLES AND SEND
BIOELECTRICITY CUES THAT
ACTIVATE THE MUSCLES...

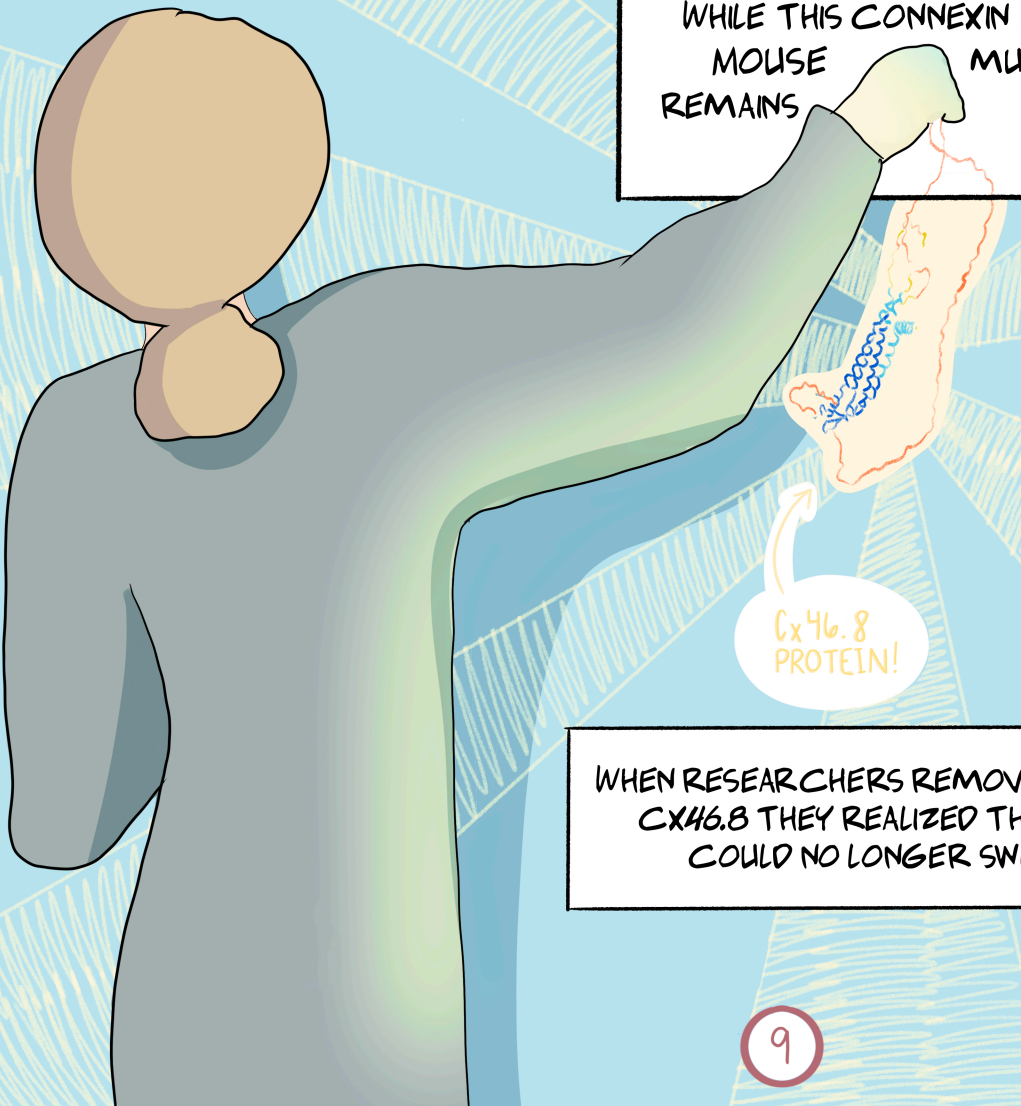


...ALLOWING FOR
CONTRACTIONS.

RESEARCHERS LOOKED FOR CONNEXINS IN THE ZEBRAFISH NEUROMUSCULAR SYSTEM AND FOUND ONE THAT HADN'T BEEN STUDIED BEFORE, CALLED GJD4/CX46.8.

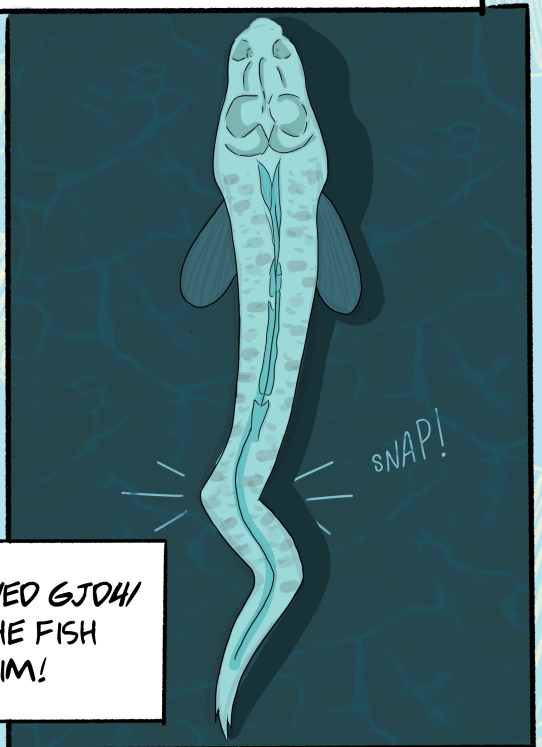


WHILE THIS CONNEXIN IS FOUND IN ZEBRAFISH AND MOUSE MUSCLE CELLS, THE FUNCTION REMAINS UNKNOWN IN HUMANS.



Cx46.8
PROTEIN!

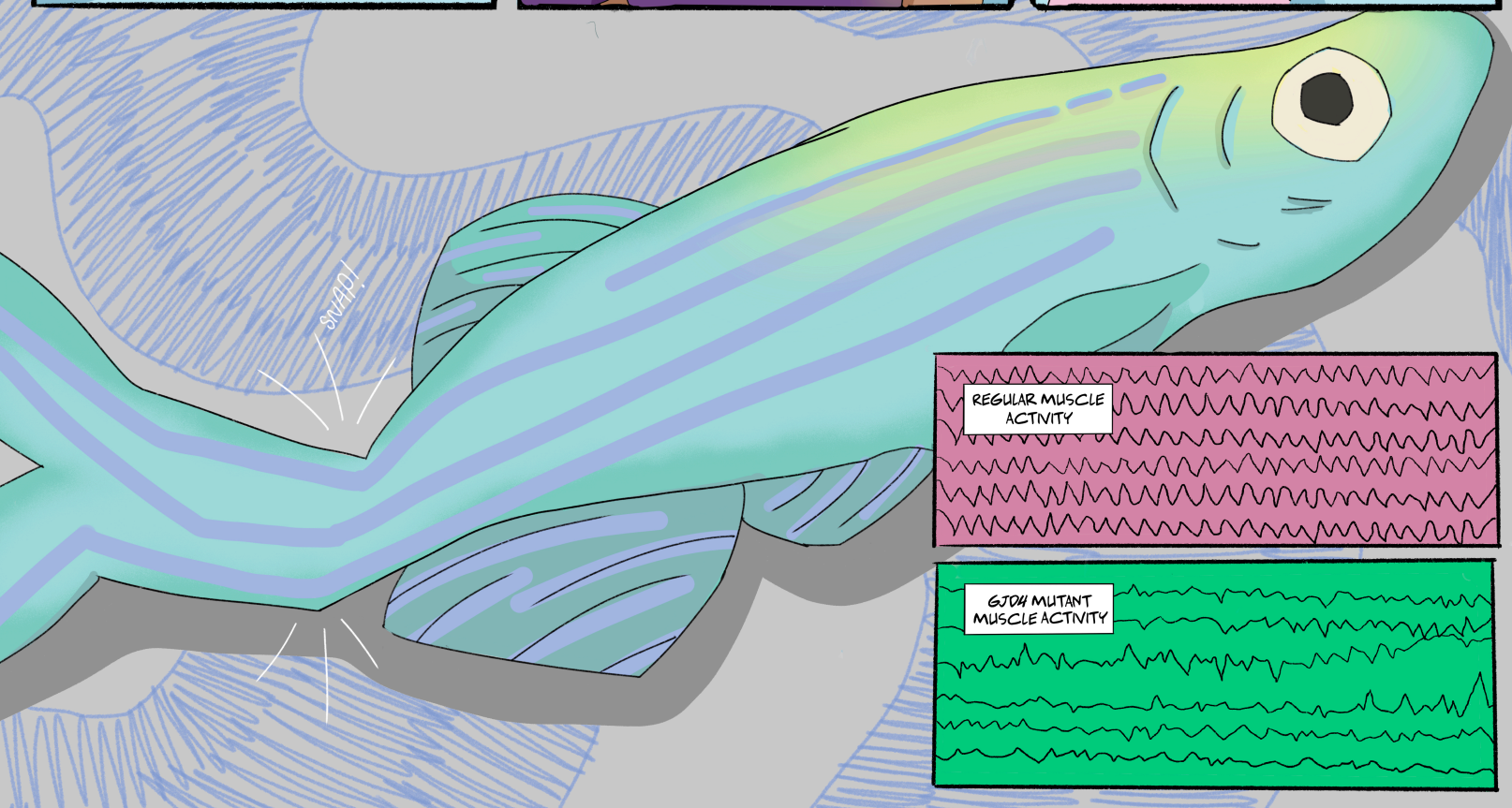
WHEN RESEARCHERS REMOVED GJD4/CX46.8 THEY REALIZED THE FISH COULD NO LONGER SWIM!



RESEARCHERS FOUND A DISRUPTION TO THE PATTERN OF BIOELECTRICITY IN THE ANIMALS THAT LACK GJDH/ CX46.8

GJDH/CX46.8 FORMS GAP JUNCTION CHANNELS THAT DIRECT SMOOTH BIOELECTRIC FLOW AMONG MUSCLE CELLS...

...RESPONDING TO MOTONEURON COMMANDS, ENSURING SMOOTH CONTRACTION AND FUNCTION.



REGULAR MUSCLE ACTIVITY

GJDH MUTANT MUSCLE ACTIVITY

WITHOUT GJDH/CX46.8, AND BIOELECTRIC SIGNALING, THE INDIVIDUAL MUSCLE FIBERS BECAME WISPY, WAVY, AND CRINKLY, HIGHLIGHTING THE IMPORTANCE OF BIOELECTRIC SIGNALING AND GAP JUNCTIONS IN DEVELOPMENT.

WHILE WE STILL DON'T KNOW THE EXACT FUNCTION OF GJD4 IN HUMANS, EARLY EVIDENCE SUGGESTS IT MAY HAVE A SIMILAR ROLE IN MAMMALS...

... THIS FINDING COULD LEAD TO A NEW ROAD FOR DISCOVERY OF GAP JUNCTIONS AND NEUROMUSCULAR DISEASES LIKE ALS, SMA, AND MUSCULAR DYSTROPHY.



ALS

- PROGRESSIVE DEGENERATION OF NERVE CELLS IN THE SPINAL CORD AND BRAIN

SMA

- AFFECTS THE MOTONEURONS, MAKING MUSCLES UNABLE TO RESPOND TO SIGNALS FROM NERVES

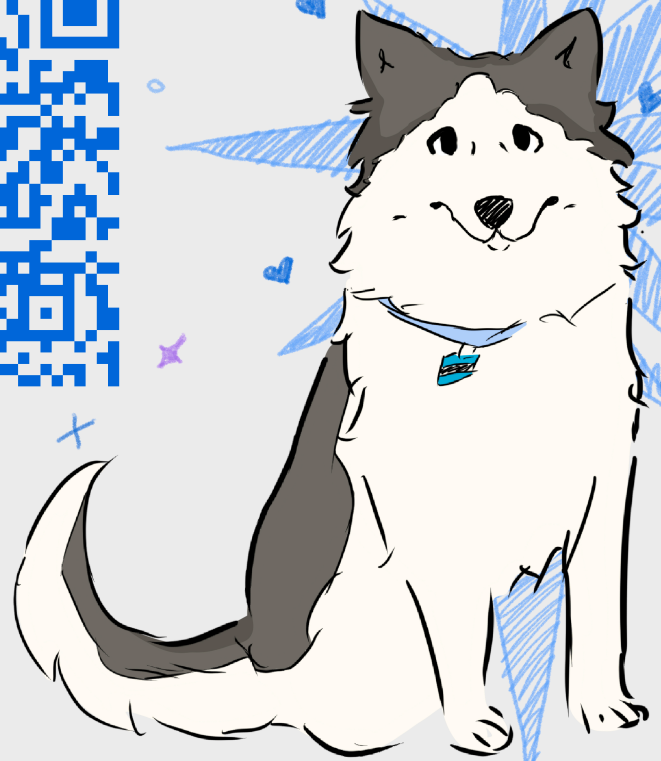
MUSCULAR DYSTROPHY

- WASTING AWAY OF MUSCLE TISSUE, WITH OR WITHOUT THE BREAKDOWN OF NERVE TISSUE



THESE LITTLE ZEBRAFISH ARE A FOUNDATIONAL STEPPING STONE FOR TESTING HUMAN TRAITS, GENES, DISEASES, AND EVEN MUSCULAR ISSUES IN HUMANS!

For more on Bentley
Smallwood's work



THANK
YOU FOR
READING!

Scan me!



Scan
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For more on Dr.
Rachel Lukowicz-
Bedford's study