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Anatomics Presents:
Issue #1: "T-Cell Training Day" Pages 1-6
By: Isaac Fisher

PAGE 1:

SYNOPSIS: Our Intrepid T-Thymoscout arrives at Fort Thymus. Hops off train. And into line.

GLOBAL NOTE: The setting is a fusion of a Vietnam War Era basic training facility stuck on top of thymus tissue. There should always be some kind of lattice of capillary networks that comprise the inside of the thymus. The ground, which is thymic epithelium, should be generally smooth with little protein-like pebbles on it. They are generally what lies on the thymic epithelium. Our Progenitor Cell comes in as an undifferentiated blob. Our Drill SGT Regular T, should look like a progenitor cell, except that his jaw is squared off and he is in full drill sergeant regalia.

PANEL ONE: At the top of our panel is an introductory title. It says Anatomics Presents: T-Cell Training Day. We then descend the page into panel 1's image. This panel is a full shot of the entire thymus. In the foreground a train labeled Progenitor Cell Express zooms towards the distant walnut shaped gland. The heart sits below and we can also catch some suggestions of the lung.

PANEL TWO: The train pulls up at the Cortico-Medullary Junction. Establishing shot here from a high angle so that we can see the entirety of Fort Thymus. We can see little progenitor cells hopping off the train and forming rows. We also have view of jeeps, and militarily attired thymocytes. Our sky and foliage comprises of a capillary network of the vasculature that surrounds the corticomedullary junction. It looks something like a lattice.

PANEL THREE: Zoom into full shot of our intrepid THYMOSCOUT. He has just hopped off the train, which we can see behind him. He holds a briefcase in hand filled with clothing and a PSGL 1 Punch Card. He looks somewhat like an undifferentiated cell. Mainly a smooth surface but has three longish hairs on top of his head. He is smiling and cheery.

PANEL FOUR: OTS shot of our Thymoscout with briefcase in hand. He follows the other Thymoscouts towards a grouping of scouts lined up to hand their PSGL-1 cards to a P-Selectin Agent. In the distance we can see a podium and building.

1) P-SELECTIN: Good Afternoon Thymoscouts. My Name is Lieutennant P-Selectin. Please hand me your Platelet Selective Glycoprotein Ligand 1 cards before proceeding.

PAGE 2:

SYNOPSIS: On this page we are introduced to SGT Killer T. He gives a motivating speech to the thymoscouts until panel 3. Then he becomes the narrator for the rest of the story's captions. In panels 4,5,6 our scouts go through their Double Negative Stage. There they get their boots, haircut, and uniforms before arriving at the Subcapsular Zone of the Thymic Cortex.

PANEL ONE: Wide Panel, Full Shot. The intrepid thymoscouts are lined up in front of a building that says Welcome to the Immune System. The building is draped with flags and other kinds of patriotic regalia. On the left side is a thymocyte dressed in a SGT uniform. He gives the run-down to the scouts.

1) SGT Killer T: All right Thymoscouts, listen up. My name is SGT. Regular T. Welcome to the Immune System. I don't know why you got here, what your background is and frankly I don't care. It is my job to make sure that you do your job right. Right now you are a motley crew of progenitor cells. Weak, Untrained, unspecific. But by the time we're through with you, you'll be an official *thymocyte*, ready to handle any of the body's foreign invaders.

PANEL TWO: Close up on our SGT. His face is menacing.

2) KILLER T: That is if you survive basic training.

PANEL THREE: MCU of our Thymoscout's Reaction. We can see his fellow thymoscouts in rank around him.

3) INTREPID THYMOSCOUT: Gulp!

PANEL FOUR: Thymoscout sits inside a barber shop and gets his head shaved. Med shot.

5) CAPTION (Killer T-): Once inside the Parenchyma, you will begin your development through the Double Negative Stages.

PANEL FIVE: Thymoscout gets his combat boots. Close up on boots. Worm's Eye View, upshot so that we can see the boot in the foreground and our Scout in the Middle Ground.

7) CAPTION: Your Drill SGT will provide you with the proper *notch signaling* to receive your basic instructions.

PANEL SIX: Thymoscout puts on his helmet. Medium Close Up shot.

10) CAPTION: And guide you through the cortex.

PAGE 3:

SYNOPSIS: On this page. Our DN thymoscouts are sent off to the outer region of the cortex where they check in with CCR9 and go through a second round of training. On this page our intrepid scout and crew make a bed. Assemble their Pre TCR Complex. And Proliferate. They receive their CD4+ and CD8+ co-receptors making the rank of DP thymoscout.

PANEL ONE: Full shot of thymoscouts marching to the outer cortex. In the BG is a barrack like structure. They march rank and file wearing their combat boots and helmets.

- 1) **CAPTION:** Next you will follow Chemokine Receptors CXCR4 and CCR7 to the outer region of the cortex.

PANEL TWO: In this panel we have another full shot. A drill SGT is pointing at a wrinkled bed and spraying spit into the face of our thymoscout hero with his shouting.

- 2) **CAPTION:** Where you will report to SGT Chemokine CCR-9.
- 3) **SGT Chemokine CCR-9:** You call that a bed, Double Negative!

PANEL THREE: Full shot. Two thymoscouts in the FG assemble their PreTCR complexes. It looks as though they are assembling M-14 guns in a field. Our drill SGT hovers over them to overlook their progress.

- 4) **CAPTION:** Along the way, you will learn to assemble your Pre-TCR Complex.

PANEL FOUR: Close up on the Pre TCR complex assembly. The PreTCR complex should look something like a hybrid between a gun with bayonet, a key, and a complex protein.

- 5) **CAPTION:** Better learn to assemble this perfectly. Your Life will depend on it!

PANEL FIVE: In the process of proliferation. Our Intrepid Thymoscout splits into two scouts. We see another split into two in the background.

- 6) **CAPTION:** Now that you've assembled your Pre-TCR Complex, it's time for proliferation. That means more of you maggots!

PANEL SIX: Now with more crowded ranks. Our Thymoscouts salute the drill SGT Killer T holding their Pre TCR complexes. OTS of SGT looking down at the thymoscouts.

- 7) **SGT Regular T:** Congratulations Scouts. You have now made it to the Double Positive Stage of your training.

PAGE 4:

SYNOPSIS: On this 8 panel page, our DN thymoscouts now have made the rank of DP thymoscouts. The SGT tosses out their CD4+ and CD 8+ coreceptors. Our thymoscout successfully makes his TCR complex. And the we jump into the grizzly selection process where most of the thymoscouts will die. Only a few scouts survive to the point of the last panel on this page.

PANEL ONE: The drill SGT passes out CD4+ and CD8+ co-receptors to our newly ranked DP thymoscouts. One scout in the foreground sticks them onto his helmet.

1) SGT: Here are your CD 4+ and CD 8+ receptors.

PANEL TWO: Our thymoscout focuses intensely while assembling his final TCR complex. The Drill SGT stands over his shoulder. Our Scout is blindfolded.

2) SGT: Now let's see you assemble that TCR Complex!

PANEL THREE: Our Thymoscout triumphantly raises his TCR complex in the air. Speed lines of celebration. In the foreground we see our drill SGT, indicated by his hat, say well done.

3) SGT: Well Done, Double Positive.

PANEL FOUR: Our thymoscouts leap into action as they make way back to the Cortical Thymic Epithelial Cells. These cells look something like trees/capillaries. We look at our scouts from a high angle and can see cells jabbing MHC complexes in the distance.

4) CAPTION: Now you will make way to the Cortical Thymic Epithelial Cell course to begin the process of selection.

PANEL FIVE: Shot of Thymoscout aggressively winding up to bayonet his MHC complex. Moment before.

5): THYMOSCOUT: Raaaaaaa!

PANEL SIX: Zoom out to Full shot of our thymoscout hero sticking his TCR complex into an MHC complex. He is looking over his shoulder in shock as he sees that one of his overly eager cadets has exploded in apoptosis.

6) CAPTION: At this stage, those of you overly avid scouts will be deleted through apoptosis.

7) THYMOSCOUT: Charlie?

PANEL SEVEN: We now look over the shoulder of our hero and come into another view of a disheveled, starving thymoscout. His TCR was poorly assembled and will not fit into the MHC complex. There are also exploded remains of apoptosized thymoscouts. Full shot.

8) CAPTION: And most of you will fail to receive your signals and die from neglect.

9) NEGLECTED T-Cell: Help! My TCR complex won't fit!

10) SGT: Forget about him.

PANEL EIGHT: Our scout looks left and right and asks, where'd everyone go? In the FG the drill SGT salutes our scout.

11) CAPTION: Those of you who interacted with low avidity will be positively selected for survival. Only 3-5% of you will survive this checkpoint of your training.

12) THYMOSCOUT: Where'd everyone go?

PAGE 5:

SYNOPSIS: On this page we begin with our remaining thymoscouts heading back to the medulla for their 12-day central tolerance training before deployment. Many more scouts will die in this exercise, however we will save the carnage for the first panel of the next page.

PANEL ONE: Full shot of our scout. He has just differentiated. He and his partner each hold a different receptor. Our scout's clone places the CD 8+ receptor on his head. Our hero holds the CD4+ receptor. He is a helper T-Cell. In the background we see our remaining thymoscouts differentiating (splitting into two).

1) **CAPTION:** Now that you are positively selected DP Thymoscouts, you will gain expression of CCR- α and differentiate into CD4+ and CD8+ Single Positive Thymoscouts.

2) **CD8+ (Killer T):** Hey CD4+, help me put this on.

PANEL TWO: Long shot. Long march from the outer cortex to the medulla. We can see the building/structure of the medulla in the distance. OTS of our scouts marching.

3) **CAPTION:** It's time to head back to the medulla. For your twelve-day central tolerance training before deployment.

PANEL THREE: The scouts shuffle into the central tolerance training area by dendritic cells who stand at the door. This is a quasi establishing shot.

4) **CAPTION:** Here you will be introduced to self-antigens by dendritic cells.

5) **DENDRITIC CELL 1:** Welcome to your central tolerance training, SPs.

6) **DENDRITIC CELL 2:** We'll be sure to take great care of you.

PANEL FOUR: Dendritic cells from high above the thymoscouts lob in grenade shaped proteins. These are self-antigens that the thymoscouts need to tolerate or else they will be deleted.

5) **DENDRITIC CELL 2:** Great Care

PANEL FIVE: Medium shot of a group of thymoscouts picking up the self-antigens that were thrown in by the dendritic cells. The antigens are spewing a little gas. They look like cannisters. A scout crouches in front of the smoking cannister.

6) **THYMOSCOUT:** What is this?

7) **THYMOSCOUT 2:** Don't pick it up!

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PANEL SIX: Close up of the self-antigen in the hands of a thymoscout. It's reacting in his hand. The antigen label reads. Brought to you by AIRE+ Expressing Medullary Thymic Epithelial Cells.

8) THYMOSCOUT: Uh-oh!

PAGE 6:

PANEL ONE: Establishing shot. Carnage. Everywhere. We see mushroom clouds of exploding thymoscouts. Blood, guts, the whole nine yards. It's like saving Private Ryan in one large panel. Our two heroes, CD 8+ and CD4+ crawl into the foreground escaping the carnage. In this distance we see one t-cell dragging a wounded comrade. On this panel, the caption is at the bottom of the image.

1) CAPTION: Many of you tissue-specific antigen reactive T-cells will be deleted. Some of you will survive.

PANEL TWO: A helper CD4+ Thymoscout drags his fellow cell (the one who picked up the antigen can.). His legs are blown off, his TCR complex is a mess, and his co-receptor is in complete disarray. (See if this can be combined with Panel 1).

2) CAPTION: A select few of you will have the honor of becoming Regulatory T-Cells.

3) THYMOSCOUT: Sarge, this CD 4+ SP is wounded. What should we do?

4) SGT: Bandage him up, and get him back to camp. This SP is now on regulatory duty.

PANEL THREE: Somehow, our hero has survived. He looks battered and bruised but also filled out. . He stands in formation with his fellow surviving thymoscouts. He is in FG. We also see jeeps and military commanders in the MG and BG.

5) CAPTION: Congratulations Thymoscout. You arrived at Fort Thymus and completed your basic training. You are now equipped with the Know-how and tools to carry out any kind of immune response.

PANEL FOUR: Our thymoscout receives a badge from a commanding officer, showing that he made the rank of Helper T-Cell. Badge says Helper T.

6) CAPTION: It's time to go back to the corticomedullary junction where you will board the post capillary vanules and await your deployment.

PANEL FIVE: Our thymoscouts board the trucks back at the corticomedullary junction where they ready for deployment. Mid shot from the perspective of the truck OTS.

7) Killer T: Helper T! Good to see you buddy! Looks like we're in the same battalion.

8) Helper T: Hop on in Killer T! We're just about to leave for combat.

PANEL SIX: Medium shot of our intrepid thymoscout and his buddy sitting at the back of the truck. They make a final punch line. Below them and "pasted" on top of the panel is a banner that says. Next Episode: It Came From Planet HIV!

9) HELPER T: Do you know anything about the enemy?

10) KILLER T: What's to know? All I know is that when I sees 'em I'm gonna kill 'em. (I'm gonna give 'em a taste of ol' cytotoxicity.

