ステムセルエイジングから解明する疾患原理

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研究成果報告書

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はしがき

加齢に伴い発症する疾患には、組織の生理的変化である老化が深く関与する。超高齢社会に急増する加齢関連疾患に対応し健康長寿を実現するためには、生理的な老化と加齢関連疾患の統合的な理解が必須である。このような中、近年の幹細胞研究の目覚ましい進歩は、多くの組織が幹細胞システムによる絶え間ない再生機転により維持されていることを明示した。一方、不老と考えられてきた幹細胞には寿命があり、幹細胞あるいは幹細胞ニッチの加齢変化（ステムセルエイジング）が、加齢関連疾患の重要な要因であることが明らかになりつつある。そこでわれわれは、近年の幹細胞研究の成果を超高齢社会における『老いと病』という重要課題に結集し、ステムセルエイジングという新しい研究領域の確立を通して、課題の解決を図る必要性があると考えた。すなわち、この新しい幹細胞研究の成果を基盤に、“ステムセルエイジング”という視点から老化、加齢関連疾患を検証し、『老いと病』という今日的命題の解決に挑んだ。この目的のために、我が国が強みとする幹細胞や老化、疾患などの研究領域を統合し、超高齢社会のニーズに対応した新領域を構築するとともに、海外の活発な老化研究との連携を推進した。

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交付決定額（配分額）

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平成 27 年度	296, 140, 000 円	227, 800, 000 円	68, 340, 000 円
平成 28 年度	298, 350, 000 円	229, 500, 000 円	68, 850, 000 円
平成 29 年度	296, 270, 000 円	227, 900, 000 円	68, 370, 000 円
平成 30 年度	297, 960, 000 円	229, 200, 000 円	68, 760, 000 円
総計	1, 509, 690, 000 円	1, 161, 300, 000 円	348, 390, 000 円

研究発表

雑誌論文（すべて査読あり、研究代表者・分担者に下線）

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特許

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発明の名称：脱毛および白毛化を抑制もしくは改善するための組成物ならびにその使用

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２．研究成果の概要

研究領域をステムセルエイジングの特性（A01）と加齢関連疾患とステムセルエイジング（A02）にわけ、A01 と A02 で得られた成果を相互に検証し合う重層的な構成をとることにより、研究の効率化と多面的な展開の実現を目指した。A01 では、幹細胞ならびにニッチの加齢変化の特性が多くの幹細胞システム（造血幹細胞、毛包・色素・表皮幹細胞、腸管上皮幹細胞、骨格筋幹細胞、神経幹細胞、精子幹細胞）について明らかとなるとともに、様々な加齢ストレス（エピゲノム異常、ゲノム異常、DNA 損傷応答、ニッチ因子の減少、代謝異常、骨髄障害ストレス, 細胞老化随伴分泌現象、感染、炎症、高脂肪食、糖代謝など）のステムセルエイジングへ影響が明らかにされ、ステムセルエイジングの特性の本体に迫る成果が得られた。また、多くの課題が A02 と連動する成果に発展した。A02 では、慢性炎症による腸管上皮幹細胞の加齢変化とゲノム変異獲得の実態解明や、ヒト大腸腫瘍オルガノイドを用いた新規解析法の開発、血管老化によるステムセルエイジングの実態解明、クローン造血モデルマウスの作成と解析、新規筋再生法の開発など、多くの成果が得られた。領域内共同研究による数理モデリングも、幹細胞を頂点とした組織の頑強性の評価系の構築などに成果が得られた。経時的な臨床検体を用いた解析も実施し、加齢に伴い変異を獲得した造血幹細胞がクローン拡大するクローン造血と骨髄球系腫瘍発症の関連の解明や、早老症 Werner 症候群患者のクローン造血の実態が明らかとなった。これらの成果は、老化の本質と疾患原理に新たなパラダイムを創出するものであり、加齢関連疾患の発症機序・病態にステムセルエイジングの観点の重要性を認識させるものとなった。