「進化の制約と方向性
～微生物から多細胞生物までを貫く表現型進化原理の解明～」

領 域 番 号：3902

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研究成果報告書

令和５年４月

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総計	1,608,620,000 円	1,237,400,000 円	371,220,000 円

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【図書】

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【研究成果による産業財産権の出願・取得状況】

１．　取得済み　トランスクリプトーム推定装置およびトランスクリプトーム推定方法、特許、特許第6993682 号　発明者：若本祐一、小林鉱石　出願年：2017　権利者：国立大学法人　東京大学　取得年：2021　国内

２．　取得済み　TRANSCRIPTOME ESTIMATION DEVICE AND TRANSCRIPTOME ESTIMATION METHOD、特許、US 10,379,052 B2　発明者：Yuichi Wakamoto, Koseki Kobayashi　出願年：2018 権利者：The University of Tokyo　取得年：2019　海外

研究成果

本領域では、個体間差や環境変化による表現型変化、発生上の揺らぎなど、短期的時間スケールで観察される表現型揺らぎを定量し、長期的な時間スケールで起こる表現型進化の制約や方向性との関係を実験的に解析、それに基づき、揺らぎ応答進化理論の検証と修正を行い、制約進化理論を構築する。その目的に向けて、[研究項目 1] 表現型の揺らぎ・環境応答の定量解析、[研究項目 2] 進化的制約・方向性の定量解析、[研究項目 3] 制約進化理論の構築、の 3 項目のもとに研究を行うこととした。進化学全体における普遍的な原理を探求するため、分子から生態系レベルにわたる多様な生物材料と、多様な進化現象（遺伝子発現プロファイル進化、環境耐性進化、発生進化、共生進化等）を対象とした。

【研究項目１】 表現型揺らぎと環境応答・進化応答を定量するため、各班が異なった生物材料を用いて研究を進めた結果、領域発足前は大腸菌を用いた実験（下記古澤班）のみにより妥当性が示されていた揺らぎ応答進化理論が、分子進化（下記市橋班）、個体発生（下記入江班）など様々な階層において成り立つことが示され、当初目的を達成した。

【研究項目２】 進化の時間スケールの異なる大腸菌、出芽酵母、脊椎動物を用いて、表現型進化がどのように制約をされているかを定量的に解析し、その背後にあるメカニズムを推察できるデータ取得を実現、その進化的制約からの逸脱がどのように生じるかに関して新たな知見を得ることに成功した。例えば、大腸菌ではどの薬剤に耐性になるかに制約がかかっていたが、それは、転写因子による制御のバランスに由来していることがわかった。さらに、脊椎動物の発生過程では、器官形成期に環境変動や突然変異よる変化表現型変化が小さいという制約がかかっていたが、これは、異なる発生ステージ間の制御遺伝子の使いまわしに由来していることがわかった。以上から、さまざまな生物における異なった時間スケールの進化において生じる制約は、どれも遺伝子制御ネットワークにおけるバランスによって引き起こされている可能性が高いことがわかり、当初目標を達成した。

【研究項目３】　金子班を中心として行われた理論的研究に加え、金子班・古澤班・倉谷班・大林班の共同研究により、揺らぎ応答進化理論の適用範囲が進化過程を経ることによって拡大することがわかった。そして、従来の揺らぎ応答進化理論に、異なる階層間の相互作用を加えることで、細胞内の分子集団やホストーパラサイト系などの生態系において、表現型進化の制約や進化のしやすい方向性を定量的に推定できるようになった。

以上のように、表現型の揺らぎと進化の制約・方向性について、分子レベルから生態系レベルまで様々な階層での定量解析が進み、揺らぎ応答進化理論が広い範囲で成り立つことが示された。さらに、表現型の少数自由度への制約や階層進化理論など、従来の揺らぎ応答進化理論を超える枠組みの構築に成功した。本領域の申請時には、計画班により細胞レベルから動植物などの多細胞レベルの解析が計画されていたが、公募班の参入により、分子レベル（市橋班・上野班）や微生物生態系（細田班）など、当初の予定を超えた多様な階層において、表現型揺らぎと進化的制約の関係が明らかとなった。これらの結果は、設定目標を予定通り達成するとともに、今後の進化学に大きな影響を与える包括的な進化理論の構築をもたらしたことから、目標を達成できたと判断している。