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研究課題名（和文）ナノカーボン物質と生体との相互作用機構の解明と生体機能材料への展開

研究課題名（英文）Design on the surface properties of nano carbon materials, and evaluation of interaction between bioactive compounds: for application of functional biomaterials

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研究成果の概要（和文）：フラーレンやカーボンナノチューブなどナノカーボン物質に対して表面化学修飾を施し、親水性の付与など様々な表面性状を持つナノカーボン物質を作成した。得られた物質とタンパク・糖鎖・DNAなど生体関連物質との相互作用を評価し、その反応機構の解明を試みた。また得られたナノカーボン物質の細胞毒性、生体適合性や体内動態を検討した。更に、ナノカーボン物質の体内動態追跡を実現するために、蛍光・磁性ラベル化など表面化学修飾ナノカーボンの作成や、化学修飾によるラベル化を必要としない生体内に存在するＣＮＴの直接観察にも成功した。

研究成果の概要（英文）：In this study, nano carbon materials such as fullerene or carbon nanotube were modified of their surface properties based on chemical modification reaction. The obtained several types of nano carbons were investigated on the interactions between biomaterials such as proteins depending on their surface properties. Their biodistribution and biocompatibility were estimated. The obtained functional groups on the surface can allow to secondary modification for applications such as drug driveller or bioimaging by emission. A Newly direct bioimaging method without any chemical modification was also succeeded based on Raman spectroscopy.

研究分野：生体材料工学

キーワード：生体適合性　ナノカーボン材料

１．研究開始当初の背景

フラーレンやカーボンナノチューブ(CNT)に代表されるナノカーボン物質は夢の材料と期待され、様々な応用展開が試みられているが、バイオ・医療分野への応用に関しては水系への分散性の確保、その生体適合性、体内動態が十分に解明されておらず、実用化の大きな妨げになっている。研究代表者の阿部は、この問題を解決すべく親水性ナノカーボン物質を開発し、タンパク等の生体物質との相互作用機構について実験的手法・理論計算に基づき、検討してきた。次いで、それらを細胞・実験動物へと投与して、生体適合性の評価を行ってきた。

ナノカーボン物質は、表面への化学修飾が容易な事や、その「グラファイト籠」としての機能など優れた特性を有するため、バイオ・医療分野を始めとする幅広い領域への応用展開が期待されている。しかし、CNT においてはそのアスベストに類似した形状から、中皮腫を誘発する可能性が疑われた事があるなど、バイオ応用への展開のためにはこれらナノカーボン物質の生体安全性・体内動態を検証する必要があるが、未だ十分な知見は得られていない。一方、ドラッグデリバリーシステム(DDS)の治療効率を格段に向上するためにも、投与するナノマテリアルの体内動態を分子生物学的に解明する必要がある。

２．研究の目的

フラーレンやカーボンナノチューブなどナノカーボン物質のバイオ応用のため、①化学修飾による親水性・機能性を付与したナノカーボン物質の開発、②得られたナノカーボン物質とタンパク・糖鎖・DNA など生体関連物質との相互作用機構（吸着・会合・離脱挙動など）を検討した。更に、③ナノカーボン物質の細胞毒性、生体適合性や体内動態の解明、表面性状の効果の検討、④体内挙動の直接的観察法の開発など、を通してドラッグデリバリーシステム(DDS)・薬剤徐放性材料など医療応用を志向した生体機能材料への展開を試みた。

３．研究の方法

フラーレンやカーボンナノチューブなどナノカーボン物質に対して表面化学修飾を施し、親水性の付与など様々な表面性状を持つナノカーボン物質を作成した。得られた物質とタンパク・糖鎖・DNA など生体関連物質との相互作用を評価し、その反応機構の解明を試みた。また得られたナノカーボン物質の細胞毒性、生体適合性や体内動態を検討した。上記で得られた生体関連物質との相互作用や、表面修飾部位を基点とした２次修飾により、DDS・薬剤徐放性材料など医療応用を志向したナノカーボン生体機能材料への展開を試みた。更に、ナノカーボン物質の体内動態追跡を実現するために、１）蛍光・磁性ラベル化など表面化学修飾ナノカーボンの作成や、２）ラベル化を必要としない顕微ラマン分光法による臓器の直接観察法の開発も試みた。

４．研究成果

今研究課題を通じ、

・表面化学修飾の結果、濃度 80 mg/L で２週間以上凝集・沈殿を生じない化学修飾 CNT の作成に成功している(図１)（論文リスト２０など）

・同じ炭素素材のグラファイトと比較して、CNT が細胞やタンパクを強く吸着することを明らかにした(図２)（論文リスト１３など）

・得られた表面修飾ＣＮＴに対して、蛍光性錯体によるラベル化を行い、蛍光性ＣＮＴの合成に成功した。(図３)（学会発表リスト１３など）

・顕微ラマン観察法を用い、臓器内 CNT の検出への展開に成功した。(図４)（論文リスト２８など）

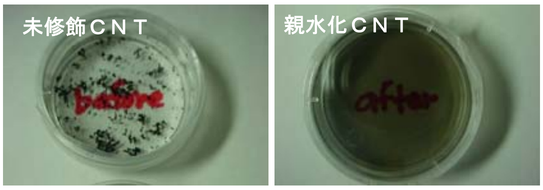

図１　表面化学修飾によるＣＮＴの分散状態の改善

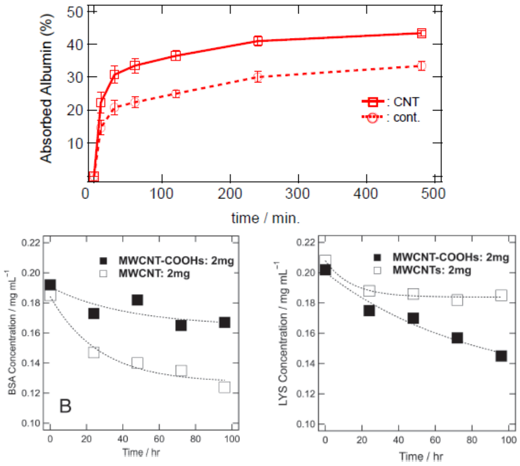

図２　各種タンパクの各種ＣＮＴへの吸着挙動

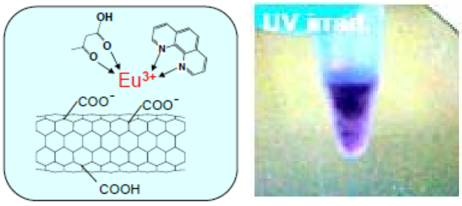

図３　遷移金属錯体を用いた蛍光ラベル化ＣＮＴ

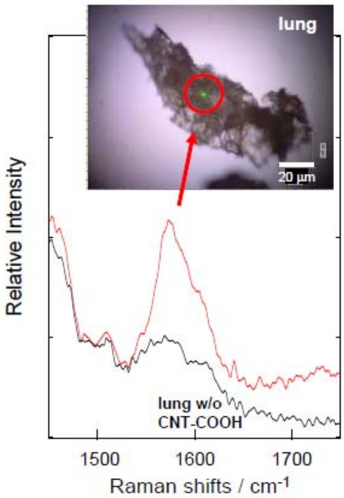

図４　顕微ラマン法による投与ＣＮＴの直接観察例（マウス肺）

５．主な発表論文等
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〔図書〕（計　０件）

〔産業財産権〕
○出願状況（計　０件）

〔その他〕
http://www.den.hokudai.ac.jp/seitaizairyou/index.html

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